DISSERTATION ON

A STUDY ON THE CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA

Submitted in partial fulfilment of

Requirements for

M.D.DEGREE EXAMINATION

BRANCH-I GENERAL MEDICINE

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI-3.

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

APRIL 2011

CERTIFICATE

This is to certify that the dissertation entitled "**A STUDY ON THE CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA** " is a bonafide work done by **DR.M.MYVIZHI SELVI**, post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai-3 in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under our guidance and supervision, during the Academic period from January 2010 to August 2010.

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ACKNOWLEDGEMENT

I thank **Prof. J.MOHANASUNDARAM, M.D., DNB, Ph.D.,** Dean, Madras Medical College, for having permitted me to conduct the study and use the hospital resources in the study.

I express my heartfelt gratitude to **Prof.C.RAJENDIRAN, M.D.,** Director, Institute of Internal Medicine for his inspiration, advice, and guidance in making this work complete.

I express my deep gratitude to my chief **Prof. A.RADHAKRISHNAN, M.D.,** Professor of Medicine, Institute of Internal Medicine for his comments, corrections and guidance to complete the study.

I am extremely thankful to Assistant Professors of Medicine **Dr. HARIDOSS SRIPRIYA VASUDEVAN, M.D., Dr. R. KALPANA, M.D., Dr. JAYAKUMAR, M.D.,** for their co-operation and guidance.

I thank **Dr.T.USHA, M.D., D.M.,** Associate professor, Department of Clinical hematology for her guidance and cooperation in the study.

Last but not the least, I would wish to thank all the patients without whose kind cooperation, this study would not have been possible.

ABBREVIATIONS

FOL	-	Folate
MDS	-	Myelo Dysplastic Syndrome
PCV	-	Packed cell volume
MCV	-	Mean Corpuscular Volume
MCHC	-	Mean Corpuscular Hemoglobin Concentration
MCH	-	Mean Corpuscular Hemoglobin
ESR	-	Erythrocyte Sedimentation Rate
RPI	-	Reticulocyte Production Index
HIV	-	Human immuno deficiency virus
HBV	-	Hepatitis B Virus
HCV	-	Hepatitis C Virus
HBsAg	-	Hepatitis B surface antigen
TSH	-	Thyroid stimulating hormone
CLD	-	Chronic liver disease
EHPO	-	Extra Hepatic portal vein obstruction

SLE	-	Systemic lupus erythematosis
CTD	-	Connective tissue disease
LDH	-	Lactate dehydrogenase

CONTENTS

INTRODUCTION

INTRODUCTION

Cytopenia is a reduction in the number in any of the three types of peripheral blood cell. A reduction in all the three types of cellular components is termed pancytopenia and this involves anemia, leucopenia, and thrombocytopenia.

Initially, mild impairment in marrow function may go undetected and pancytopenia may become apparent only during times of stress or increased demand (e.g., bleeding or infection). As severity increases, the peripheral blood count decreases even in the steady state. Peripheral pancytopenia may be a manifestation of wide variety of diseases which can primarily or secondarily affect the bone marrow.

The frequency of underlying pathology causing pancytopenia varies considerably depending upon various factors including geographic distribution and genetic disturbances. The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients with pancytopenia. The basic investigations in a suspected case of pancytopenia include Complete Blood Count with peripheral blood film and Reticulocyte count.

The presenting symptoms are usually attributable to anemia or thrombocytopenia. Red blood corpuscles survive much longer than platelets or neutrophils.Hence anaemia develops slowly (unless there is significant bleeding) and the typical symptoms of tiredness, fatigue, puffiness of face, edema, lassitude, and effort intolerance may not be striking in the initial phase.

The platelet count is first to be affected. Mucocutaneous bleeding is typical of thrombocytopenia with petechial haemorrhages in skin and mucous membranes (commonest being epistaxis, haematuria, GI bleeding, menorrhagia, and only rarely intracranial bleeding). The presence of spontaneous bleeding with platelet count $<20 \times 10^9$/l indicates severe marrow failure.

Leucopenia is an uncommon cause of initial presentation, but can cause a more serious threat to the life in its subsequent course. Infections usually occur with commensal organisms of the skin or gastrointestinal tract. Early manifestation of neutropenia is often a sore throat or chest or soft tissue infection which typically show incomplete response to antibiotics. Unfortunately, patients with pancytopenia may develop overwhelming septicemia without any focal sign of infection; the only clinical features being malaise and fever.

Pancytopenia can be due to decrease in hematopoietic cell production in the bone marrow e.g. by infections, toxins, malignant cell infiltration or suppression or can have normocellular or even hypercellular marrow, without any abnormal cells, e.g. ineffective hematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells. Bone marrow biopsy plays a significant role in understanding the etiology of pancytopenia. Hence Bone marrow examination is indicated in all cases of pancytopenia.

Pancytopenia is an important clinico haematological entity encountered in our day-to- day clinical practice. There are varying trends in its pattern, treatment modalities, and outcome. There are very few data about the clinical presentation, and the etiology of pancytopenia in Indian patients. The aim of this study to evaluate the clinical presentation and etiological spectrum of pancytopenia on the basis of peripheral smear and bone marrow examination.

Hence this study is designed to evaluate the presenting features and the causes of patients with pancytopenia.

AIMS

&

OBJECTIVES

AIMS AND OBJECTIVES

To evaluate the clinical and etiological profile of patients presenting with pancytopenia.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Pancytopenia is defined as a decrease in all cellular elements of the circulating blood, including erythrocytes, leukocytes, and platelets. The degree of decrease in any one of these elements may vary at any time in the course of the illness. Some disorders that cause pancytopenia may initially come to attention as single-cell cytopenia. Anemia is defined as hemoglobin level less than 13g/dl in men and 12g/dl in women. Thrombocytopenia is a platelet count less than 150,000 per microliter

and leucopenia is a white blood cell count less than 4,000 per microliter. Although leucopenia may be caused by lymphopenia or neutropenia, the most common finding is neutropenia with an absolute neutrophil count less than 1,500 per microliter.

PRESENTATION

Mild pancytopenia may be asymptomatic, the patient manifesting findings associated with the primary underlying disorder. Patients with severe pancytopenia come to medical attention in an explosive, life-threatening clinical scenario.

Patients with granulocyte counts less than 500 per microliter may have overwhelming sepsis. A patient with a platelet count less than 20,000 per microliter may have life-threatening, spontaneous hemorrhage. Acquired or congenital qualitative platelet dysfunction may cause increased hemorrhage. Patients may have simultaneous severe bleeding and infection. Symptoms associated with anemia often are more insidious because of the usual gradual onset of anemia. In addition to the findings of the underlying disease, findings at physical examination often are pallor, fever, necrotic abscess, and spontaneous petechiae and ecchymoses.

Severe pancytopenia is a medical emergency. Because this condition is life threatening, immediate supportive care, rapid diagnosis, and definitive and preventive treatment should be instituted. Pancytopenia is a symptom complex of an underlying disorder in which there is an absolute or relative decrease in effective hematopoietic production of peripheral blood cell elements.

PATHOPHYSIOLOGY

In general, pancytopenia results from one of four pathophysiologic processes. Absence of hematopoietic progenitors that cause aplastic anemia is thought to be synonymous with pancytopenia. However,

pancytopenia may be caused by other pathologic states. A decrease in normal hematopoiesis may be caused by replacement of the bone marrow cavity, the site of adult hematopoiesis, through a pathologic process that may be hematopoietic in origin or be caused by invasion by extrahematopoietic cells. Reactive myelofibrosis may be present. This process is called myelophthisis. Ineffective hematopoiesis results in progenitors that produce normal to increased numbers of cellular elements that are incapable of normal maturation and succumb to intramedullary destruction. This situation is manifested in severe folate or vitamin B_{12} deficiency or myelodysplasia. Pancytopenia may be caused by increased peripheral destruction of cellular elements with a hypercellular marrow incapable of adequate compensatory production. Some disorders, such as HIV infection, that cause pancytopenia may do so by more than one mechanism.

DIFFERENTIAL DIAGNOSIS OF PANCYTOPENIA

Pancytopenia with Hypocellular Bone Marrow

Acquired aplastic anemia

Constitutional aplastic anemia (Fanconi's anemia, dyskeratosis congenita)

Some of the myelodysplasias

Rare aleukemic leukemia (AML)

Some cases of acute lymphoid leukemia

Some cases of lymphomas of bone marrow

Pancytopenia with Cellular Bone Marrow

Primary bone marrow diseases/disorders

Myelodysplasia

Paroxysmal nocturnal hemoglobinuria

Myelofibrosis

Some aleukemic leukemia

Myelophthisis

Bone marrow lymphoma

Hairy cell leukemia

Secondary to systemic diseases

Systemic lupus erythematosus

Hypersplenism

Vitamin B12, folate deficiency

Overwhelming infection

Alcohol

Brucellosis

Sarcoidosis

Tuberculosis

Leishmaniasis

Hypocellular Bone Marrow +/- Cytopenia

Q fever

Legionnaires' disease

Anorexia nervosa, starvation

Mycobacteria

HISTORY AND PHYSICAL EXAMINATION

The history and physical examination often lead to the diagnosis of pancytopenia. Because of the diversity of manifestations and causes of pancytopenia, a detailed and careful history and physical examination are required. Anemia may cause increasing fatigue and dyspnea on exertion, but because of the gradual onset of symptoms, it may be insidious and not detected earlier. Among elderly patients, increasing signs and symptoms of congestive heart failure may be evident. Despite severe anemia, the blood volume may be increased. Leukopenia and neutropenia may cause unexplained high fevers, shaking chills, and repeated, persistent infections. Thrombocytopenia may come to attention as increasing ecchymoses and petechiae, particularly in the lower extremities. Patients with severe thrombocytopenia may report bleeding from their gums or oral mucosa or visual changes caused by retinal hemorrhage. Patients may have signs and symptoms of life-threatening intracranial hemorrhage. Women of childbearing age may have severe menorrhagia.

The history often determines the duration of pancytopenia. Some patients notice the gradual onset of increasingly severe symptoms, but for others, the onset is sudden and fulminant. The history may show the cause of the pancytopenia. The history of illnesses, medications, and

surgical procedures is important. That a patient has undergone gastrectomy or ileal resection suggests the possibility of vitamin B_{12} deficiency. A careful drug history, including the months before the onset of symptoms, is important in ascertaining whether the patient has drug-induced aplastic anemia. Administration of chemotherapy or high-dose radiation therapy to the bone marrow often causes expected pancytopenia of finite duration. A history of collagen vascular disease or rheumatoid arthritis suggests aplastic anemia or a lymphoproliferative disorder. The patient should be asked specifically about the presence of dark urine at the initial morning void, which suggests the presence of paroxysmal nocturnal hemoglobinuria.

A history of a malignant disease metastatic to bone marrow suggests the possibility of a myelophthisic process. The primary malignant tumor may be remote in time; recurrence comes to attention as bone marrow involvement or a more generalized process accompanied by constitutional symptoms such as weight loss and night sweats, although fever also may be symptomatic of infection due to neutropenia. Secondary hematopoietic malignant diseases or myelodysplastic syndromes may be caused by earlier chemoradiation therapy.

The history should include an adequate dietary evaluation that includes alcohol ingestion. The possibility of HIV infection should be entertained, and the history should include potential risk factors. To determine the possibility of a genetic disorder such as lipid storage disease or congenital aplastic anemia, a complete family history should be obtained. Although primarily diagnosed in childhood, these disorders may occur in young adulthood or later. A travel history should be established, because infectious diseases may cause pancytopenia.

The physical examination is important in determining the severity and consequences of pancytopenia and possibly in establishing the underlying diagnosis. In mild pancytopenia, only pallor may be observed. With serious thrombocytopenia, ecchymosis and petechiae may be noticed, particularly on the lower extremities and pressure points. In cases of severe thrombocytopenia, petechiae and bleeding also may be seen in the oral mucosa and retina. The latter findings indicate an emergency. High spiking fevers may indicate the presence of potentially life-threatening infection. Careful examination for the source of the infection must be undertaken. In the absence of neutrophils, an infected site contains necrotic ulcers. Important cutaneous microemboli and rashes may be present. Sinuses should be percussed for tenderness. A careful, noninvasive examination of the per rectal area should be performed. In

the absence of adequate neutrophils, the findings of pneumonia may be subtle.

The physical examination should be an attempt to determine the cause of the pancytopenia. In many disorders, there may be no further physical findings. However, splenomegaly may indicate that pancytopenia has been caused by hypersplenism or a myelophthisic state with extramedullary splenic hematopoiesis. With massive splenomegaly, the spleen extends into the lower abdomen, and the examination should begin in the lower abdomen and carefully proceed cephalad. Massive splenomegaly occurs in Gaucher's disease, myelofibrosis, hairy cell leukemia, and lymphoma. Splenomegaly usually does not occur with aplastic anemia, acute lymphocytic leukemia, ineffective hematopoiesis, and myelodysplastic syndromes.

Lymphadenopathy may indicate the presence of lymphoma, acute or chronic lymphocytic leukemia, or metastatic carcinoma. Examination of the breasts should be performed, because pancytopenia may accompany metastatic breast carcinoma. Skin and joint findings suggesting collagen vascular disease or arthritis may indicate the presence of immunologically mediated pancytopenia.

LABORATORY STUDIES AND DIAGNOSTIC TESTS

Laboratory studies are the most definitive aspect of the evaluation for pancytopenia. An immediate and careful examination of a good-quality peripheral blood smear is mandatory. The complete blood cell count and differential count may indicate that some cell lines are more severely affected than others. Cell lines should be individually examined.

Erythroid macrocytosis may indicate ineffective hematopoiesis, as in vitamin B_{12} or folate deficiency, or the defect may occur as leukoerythroblastosis in myelophthisic disorders. The latter condition may be associated with poikilocytosis, nucleated RBCs, and teardrop-shaped cells. Nucleated RBCs are findings of stress erythropoiesis. Although aplastic anemia is classified as normochromic normocytic anemia, macrocytosis indicative of terminal stress erythropoiesis may be present. Polychromatophilia is indicative of erythroid production.

Rouleaux formation may indicate lymphoma or multiple myeloma. Blasts may indicate an underlying leukemia or myelodysplastic syndrome. Hairy cell leukemia, chronic lymphocytic leukemia, and non-Hodgkin's lymphoma may be associated with the finding of circulating malignant cells the presence of which is enough to confirm a diagnosis. In some bone marrow failure syndromes, such as aplastic anemia, an

absence of myeloid cells causes relative lymphocytosis. A leukoerythroblastic smear has a few immature myeloid cells in addition to the RBC changes. Pelger–Huet anomaly and hypogranulation of the myeloid cells suggest an underlying myelodysplastic syndrome. Hypersegmentation of polymorphonuclear leukocytes is associated with megaloblastic anemia. An almost normal differential count and percentage of myeloid cells may indicate peripheral destruction caused by hypersplenism. Decreased numbers of small platelets indicate decreased platelet production, and the presence of giant platelets is associated with a myelophthisic process or compensatory thrombopoiesis.

Most important, examination of the peripheral blood must include a reticulocyte count with a supravital stain for numeric assessment of erythroid production. For more accurate measurement of erythropoiesis, the reticulocyte count should be corrected for an abnormal hemoglobin level.

In all cases of pancytopenia, bone marrow aspiration and biopsy should be performed immediately after the peripheral blood examination. In conjunction with the peripheral blood findings, these studies can help identify the cause of the pancytopenia in most cases. Aspirate examination of individual cell lines and cells allows the diagnosis of

malignant disease of the hematopoietic system, lipid storage disorders, megaloblastic anemias, and myelodysplastic syndromes. Metastatic cancer cells sometimes are found in the aspirate, although these findings are more frequent in core biopsy. Prussian blue stains may demonstrate the presence of the ringed sideroblasts indicative of the myelodysplastic syndromes. Examination of the aspirate should include flow cytometry, which may aid in the identification of clonal abnormal cell populations. Cytogenetic abnormalities are found in the congenital bone marrow failure syndromes, such as Fanconi's aplastic anemia, and in some types of leukemia and myelodysplastic syndrome.

Extremely important in the evaluation of pancytopenia is core bone marrow biopsy, especially if a hypocellular aspirate is obtained. The biopsy provides the only true estimate of bone marrow cellularity. Although hypocellular marrow usually is associated with aplastic anemia, the possibility of a hypocellular myelodysplastic syndrome must be considered, and the core biopsy should be carefully correlated with the aspirate biopsy and cytogenetic studies. Bone marrow biopsy allows the diagnosis of myelofibrosis and increases the yield of diagnosis of metastatic carcinoma, mycobacterial infection, lymphoma, and hairy cell leukemia. No specific marrow findings are associated with HIV infection, although some of the secondary consequences such as granuloma or

lymphoma may be demonstrated in the marrow. Bone marrow aspiration and biopsy often establish the diagnosis among patients with an enlarged spleen, particularly if the splenomegaly is caused by an infiltrative disorder or extramedullary hematopoiesis.

Careful evaluation of the peripheral blood and bone marrow often establish the cause of the pancytopenia. The need for further laboratory testing is dictated by the results of these examinations.Below are discussed some of the common causes of pancytopenia.

MEGALOBLASTIC ANEMIA

Megaloblastic anemia most commonly results from folate or cobalamin (vitamin B12) deficiency. Folate deficiency usually is nutritional in origin. It may be seen in alcoholics and the elderly poor but also is seen in patients on hyperalimentation or hemodialysis. Diagnosis is based on measurements of folate in serum, which furnishes information about the current level of folate, and in red cells, which provides data on folate levels over the preceding 6 weeks. Nutritional folate deficiency is treated with folic acid. Folate deficiency as a result of malabsorption occurs in tropical and nontropical sprue.

The most common cause of cobalamin deficiency is pernicious anemia (PA), a condition in which the portion of gastric mucosa that contains the parietal cells is destroyed through an autoimmune mechanism. Cobalamin deficiency leads not only to megaloblastic anemia but also to a demyelinating disease that manifests itself as peripheral neuropathy, spastic paralysis with ataxia (so-called combined system disease of the spinal cord), dementia, psychosis, or a combination of the foregoing. "Subtle" cobalamin deficiency, manifested as neurologic symptoms without anemia, appears to be relatively widespread among the elderly.

Definition:

Megaloblastic anemia are disorders caused by impaired DNA synthesis. The presence of megaloblastic cells is the morphologic hallmark of this group of anemias. Megaloblastic red cell precursors are larger than normal and have more cytoplasm relative to the size of the nucleus. Promegaloblasts show a blue granule-free cytoplasm and a granular chromatin that contrasts with the ground-glass texture of its normal counterpart. As the cell differentiates, the chromatin condenses more slowly than normal into dark aggregates that coalesce, giving the nucleus a characteristic fenestrated appearance. Condensation of chromatin to a homogeneous mass either fails or is delayed. The growing

maturity of the cytoplasm as it acquires hemoglobin contrasts with the immature-looking nucleus, a feature termed *nuclear-cytoplasmic asynchrony*. Megaloblastic granulocyte precursors are larger than normal. They show nuclear-cytoplasmic asynchrony, with cytoplasm that looks less mature than the cytoplasm of their normal counterparts. A characteristic cell is the *giant metamyelocyte*, which has a large horseshoe-shaped nucleus, sometimes irregularly shaped, containing ragged chromatin. Megaloblastic megakaryocytes may be abnormally large, with deficient granulation of the cytoplasm. In severe megaloblastosis, the nuclteus may show unattached lobes.

By far the most common causes of megaloblastic anemia are folate deficiency and cobalamin deficiency.

Causes of Megaloblastic Anemias

Folate deficiency

Decreased intake

Poor nutrition

Old age, poverty, alcoholism

Hyperalimentation

Hemodialysis

Premature infants

Spinal cord injury

Children on synthetic diets

Goat's milk anemia

Impaired absorption

Nontropical sprue

Tropical sprue

Other disease of the small intestine

Increased requirements

Pregnancy

Increased cell turnover

Chronic hemolytic anemia

Acute megaloblastic anemia

Nitrous oxide exposure

Severe illness with

Extensive transfusion

Dialysis

Total parenteral nutrition

Exposure to weak folate antagonists (e.g., trimethoprim or low-dose methotrexate)

Drugs

Dihydrofolate reductase inhibitors

Antimetabolites

Inhibitors of deoxynucleotide synthesis

Anticonvulsants

Oral contraceptives

Others

Inborn errors

Cobalamin deficiency

Imerslund-Gräsbeck disease

Congenital deficiency of intrinsic factor

Transcobalamin II deficiency

Errors of folate metabolism

Exfoliative dermatitis

Cobalamin deficiency

Impaired absorption

Gastric causes

Pernicious anemia

Gastrectomy

Zollinger-Ellison syndrome

Intestinal causes

Ileal resection or disease

Blind loop syndrome

Fish tapeworm

Pancreatic insufficiency

Decreased intake

Vegeterians

Congenital folate malabsorption

Dihydrofolate reductase deficiency

N^5-methyl FH_4 homocysteine–methyltransferase deficiency

Errors of cobalamin metabolism

"Cobalamin mutant" syndromes with homocystinuria

Other errors

Hereditary orotic aciduria

Lesch-Nyhan syndrome

Thiamine-responsive megaloblastic anemia

Unexplained

Congenital dyserythropoietic anemia

Refractory megaloblastic anemia

Erythroleukemia

Laboratory Features:

Peripheral smear:

All cell lines are affected. Erythrocytes vary markedly in size and shape, often are large and oval, and in severe cases can show basophilic stippling and nuclear remnants (Cabot rings, and Howell-Jolly bodies). Erythroid activity in the marrow is enhanced, although the megaloblastic cells usually die before they are released, accounting for the reduced

reticulocyte count. The more severe the anemia, the more pronounced the morphologic changes in the red cells. When the hematocrit is less than 20 percent, erythroblasts with megaloblastic nuclei, including an occasional promegaloblast, may appear in the blood. The anemia is macrocytic (mean corpuscular volume [MCV] = 100–150 fl or more), although coexisting iron deficiency, thalassemia trait, or inflammation can prevent macrocytosis. Slight macrocytosis often is the earliest sign of megaloblastic anemia.

Neutrophil nuclei often have more than the usual three to five lobes. Typically, more than 5 percent of the neutrophils have five lobes. Cells may contain six or more lobes, a morphology never seen in normal neutrophils. In nutritional megaloblastic anemias hypersegmented neutrophils are an early sign of megaloblastosis and persist in the blood for many days after treatment.Even presence of a single hypersegmented neutrophil should warrant evaluation for megaloblastic anemia. Chromosomes are elongated and broken. Specific therapy corrects these abnormalities, usually within 2 days, although some abnormalities do not disappear for months. Platelets are slightly smaller than normal and vary more widely in size (increased platelet distribution width).

Bone Marrow in megaloblastic anemia:

Aspirated marrow is cellular and shows striking megaloblastic changes, especially in the erythroid series. The high apoptosis rate of erythroid precursor cells in the marrow creates more globin lysis and, thus, jaundice. Sideroblasts are increased in number and contain increased numbers of iron granules. The ratio of myeloid to erythroid precursors falls to 1:1 or lower, and granulocyte reserves may be decreased. In severe cases, promegaloblasts containing an unusually large number of mitotic figures are plentiful.

Treatment consists of parenteral cyanocobalamin (vitamin B12) or oral vitamin B12 to replace daily losses and refill storage pools.Toxicity is unusual, although severe hypokalemia leading to cardiac arrhythmias can be seen.A typical treatment schedule consists of 1000 micrograms of cobalamin IM daily for 2 weeks, then weekly until the hematocrit is normal, and then monthly for life. For neurologic manifestations, 1000 micrograms every 2 weeks for 6 months is recommended. Higher doses are given for certain inherited disorders (e.g., TCII deficiency). Cobalamin should be given by mouth to patients with dietary cobalamin deficiency and patients (e.g., hemophiliacs) who cannot take IM injections.

Transfusion occasionally is required when the hematocrit is less than 15 percent or the patient is debilitated, infected, or in heart failure. In such instances, packed cells should be given slowly to avoid pulmonary edema. Infections can impair the response to cobalamin and must be treated vigorously.

HYPERSPLENISM

The spleen culls aged and abnormal cells from the blood; removes intraerythrocytic inclusions through a process called pitting; sequesters approximately one third of the normal intravascular platelet pool; removes bacteria, foreign particles, and tumor cells from the blood; and by virtue of the T and B lymphocytes and macrophages in the white pulp plays a role in immune surveillance and antibody formation. Exaggeration or impairment of some or all of these splenic functions results in hypersplenism or hyposplenism, respectively. Hypersplenism can be caused by splenic enlargement as a result of vascular engorgement or cellular infiltration. Splenomegaly resulting from vascular engorgement, such as portosplenal vein hypertension, or from infiltrative disease commonly leads to a combination of neutropenia, thrombocytopenia, and anemia. Hypersplenism also can be caused by moderate or minimal splenic enlargement as a result of exaggerated removal of physically abnormal (e.g., hereditary spherocytosis) or antibody-coated blood cells (e.g., immune thrombocytopenia).

Definition:

The designation hypersplenism refers to exaggeration of the spleen's normal filtration and phagocytic functions. The disorder can occur primarily by enlargement of the spleen from vascular congestion, histiophagocytic hyperplasia, cellular infiltration, or secondarily by the inability of physically abnormal red cells, such as sickle cells, or antibody-coated cells, such as in immune thrombocytopenia purpura, to navigate the circulation or avoid engulfment by the mononuclear phagocyte population of the normal spleen. Hypersplenism usually is associated with the triad of splenomegaly, blood cytopenias, and compensatory marrow hyperplasia; it is characteristically corrected by splenectomy.

Pathophysiology:

Splenomegaly increases the proportion of blood channeled through the red pulp, causing inappropriate hypersplenic sequestration of normal and abnormal blood cells.Spleen enlargement may result from expansion of the red pulp compartment in any red cell sequestration process; extramedullary hematopoiesis, notably in idiopathic myelofibrosis; hyperplasia or neoplasia involving the white pulp, such as infectious mononucleosis or lymphoma, respectively; or histiophagocytic hyperplasia.

The increased size of the filtering bed is more pronounced when the splenomegaly is caused by congestion (as in portal hypertension) than when it is caused by cellular infiltration (as in leukemias, thalassemias, or amyloidosis). Nevertheless, even in space-occupying disorders such as Gaucher disease and myelofibrosis, splenomegaly may be associated with severe hypersplenic sequestration of normal cells.

Splenomegaly increases the vascular surface area and thereby the marginated neutrophil pool. Platelets are especially likely to be sequestered in an enlarged spleen, and up to 90 percent of the total number of platelets in blood may be found in massively enlarged spleens. However, sequestered white cells and platelets survive in the spleen and may be available when increased demand requires neutrophils or platelets, although their release may be slow.

Red cells, on the other hand, often are destroyed prematurely in the red pulp. Anemia in patients with splenomegaly has been considered the result of dilution of red cells in an expanded plasma volume. However, expansion, as measured by radiolabeled albumin or fibrinogen, results more from an increase in the splenic pool of protein rather an increase in circulating plasma volume.

Varying amounts of erythrophagocytosis are present, reflecting the normal culling of senescent red cells. Erythrophagocytosis increases as a result of hemolytic anemia and viral infections, and in alloimmunized transfusion recipients. Macrophages within the sinusoids contain red cell fragments. When the process is pronounced, the littoral cells become cuboidal and stand out on the basement membrane ("hobnails"). Sickle cell disease and red cell membrane disorders such as hereditary spherocytosis lead to sequestration of the poorly deformed red cells in the cords but little extrasinusoidal erythrophagocytosis, in contrast to immune hemolytic anemia where macrophage erythrophagocytosis is prominent.

Splenomegaly with Appropriate Hypersplenism	**Splenomegaly with Inappropriate Hypersplenism**
Hereditary hemolytic anemias	Congestion (Banti syndrome)
Hereditary spherocytosis	Cirrhosis of the liver
Hereditary elliptocytosis	Portal vein thrombosis
Thalassemia	Splenic vein obstruction
Sickle cell anemia (infants)	Budd-Chiari syndrome
	Congestive heart failure
Autoimmune cytopenias	
Idiopathic thrombocytopenia	Infiltrative disease

Essential neutropenia

Acquired hemolytic anemia

Infections and inflammations

Infectious mononucleosis

Subacute bacterial endocarditis

Miliary tuberculosis

Rheumatoid arthritis (Felty syndrome)

Lupus erythematosus, Sarcoidosis

Brucellosis, Leishmaniasis

Schistosomiasis,Malaria

Leukemias, chronic and acute

Lymphomas

Polycythemia vera

Agnogenic myeloid metaplasia

Gaucher disease

Niemann-Pick disease

Glycogen storage disease

Amyloidosis

Laboratory Features:

The characteristic triad of hypersplenism is (1) splenomegaly, (2) blood cytopenias, and (3) hyperplasia of the corresponding lineage in the marrow. The blood cell morphology usually is normal, although a few spherocytes may result from metabolic conditioning of red cells during repeated slow transits through the expanded red pulp. A compensatory increase in red cell production usually is evident by an increased reticulocyte count. This finding may be quantitatively less evident because the spleen preferentially sequesters reticulocytes. The presence

of a compensatory increase in neutrophil or platelet production is more difficult to identify morphologically. Tests such as epinephrine mobilization have been used to distinguish sequestration from ineffective cellular production. Epinephrine releases neutrophils and platelets from the spleen, but the test may be difficult to interpret since epinephrine also releases the cells from marginal pools. The pathophysiology usually can be inferred from the associated clinical findings and other tests including the marrow examination.

Pancytopenia is a common finding in patients with hepatic cirrhosis and portal hypertension. However, why some patients with cirrhosis develop marked cytopenias and others do not is not clear. About one third of patients with cirrhosis develop severe hypersplenism. Decompensated liver disease and history of alcohol consumption are independent risk factors for hypersplenism. The presence of hypersplenism in patients with chronic liver disease increases the probability of variceal bleeding.

MYELOPHTHISIC ANEMIA

Myelophistic anemia refers to anemia resulting from the presence of spotty to massive marrow infiltration with abnormal cells or tissue components. the term *myelophthisic anemia* is best reserved for marrow

replacement by nonhematologic tumors and nonhematopoietic tissue. The two major features of idiopathic myelofibrosis are extramedullary hematopoiesis (in spleen, liver, and other organs) and bone marrow fibrosis. Minimal to moderate involvement usually does not cause symptoms or hematologic changes. However, such infiltration is clinically significant because in patients with an established diagnosis of cancer, it indicates metastatic dissemination of the tumor and usually an incurable disorder. Extensive infiltration may lead to pancytopenia. The condition accompanied by teardrop-shaped red cells, prematurely released nucleated red cells, and immature myeloid cells is referred to as *leukoerythroblastic reaction.* In myelofibrotic disorders of both idiopathic and secondary origin, the malignant clone releases fibroblastic growth factors. The resultant fibrosis restricts the available bone marrow space and disrupts bone marrow architecture. The disruption may cause cytopenias with production of deformed red cells, especially poikilocytes and teardrop-shaped cells, and premature release of erythroblasts, myelocytes, and giant platelets.

The anemia usually is mild to moderate, but it can be severe. White cell and platelet counts may vary, but the most characteristic feature is the morphologic appearance of red cells on the blood film. These cells may show anisocytosis and poikilocytosis, but the presence of teardrop forms

and nucleated red cells is particularly suggestive of marrow infiltration. The combination of nucleated red cells and immature myeloid precursors constitutes the leukoerythroblastic picture that is characteristic of marrow infiltration. Marrow biopsy is the most reliable procedure used to diagnose marrow-infiltrative disease and should be performed in all patients with suspected metastatic carcinoma or hematologic features of myelophthisic anemia. The inability to aspirate marrow (dry tap) leads to a high degree of suspicion of marrow replacement.

APLASTIC ANEMIA

Aplastic anemia is defined as the failure of bone marrow to produce blood cell components. The hallmarks of the disease are pancytopenia and a hypocellular bone marrow. Aplastic anemia is a rare disease. Inherited forms of the disorder are rare and consist of Fanconi's anemia, dyskeratosis congenita, and Schwachman syndrome. Among patients with the acquired disorder, idiopathic aplastic anemia, in which no cause is apparent, accounts for approximately 65% of all cases of aplastic anemia

Acquired aplastic anemia

Idiopathic

Secondary

Chemicals

Benzene

Insecticides

Glue

Solvents

Drugs

Cytotoxic agents

Antibiotics

Nonsteroidal anti-inflammatory drugs

Anticonvulsive agents

Gold salts

Radiation

Viruses

Epstein-Barr virus

Non-A, non-B, non-C hepatitis viral agent

Human immunodeficiency virus

Immune and rheumatologic diseases

Graft-versus-host disease

Rheumatoid arthritis

Systemic lupus erythematosus

Paroxysmal nocturnal hemoglobinuria

Pregnancy

Inherited aplastic anemia

Fanconi’s anemia

Dyskeratosis congenita

Schwachman syndrome.

Pathophysiology:

The pancytopenia in aplastic anemia reflects failure of the hematopoietic process manifested as a severe decrease in the numbers of all hematopoietic progenitor cells. Two mechanisms have been suggested for bone marrow failure. The first mechanism is direct hematopoietic injury by chemicals (eg, benzene), drugs, or radiation to both proliferating and quiescent hematopoietic cells. The second mechanism, supported by clinical observations and laboratory studies, is immune-mediated suppression of marrow cells

Clinical presentation:

The signs and symptoms of patients presenting with aplastic anemia are typically related to the decrease or absence of peripheral blood cellular components. The clinical presentation ranges from insidious to dramatic.

Hepatosplenomegaly, lymphadenopathy, or bone pain is less common in patients with aplastic anemia.

Diagnostic Evaluation:

The hallmark of aplastic anemia is pancytopenia and a hypocellular bone marrow. Because of the hypoproliferative marrow, the reticulocyte

response is low or absent despite the anemia. Bone marrow aspiration and biopsy must be performed to rule out other possible causes for pancytopenia, such as MDS or leukemia. In normal bone marrow, 40% to 60% of the marrow space is typically occupied with hematopoietic cells depending on the age of the person; by contrast, the bone marrow in patients with aplastic anemia typically contains very few hematopoietic cells and consists primarily of fatty space and stromal cells.

MYELODYSPLASTIC SYNDROMES

The MDS are a group of clonal hematopoietic stem cell disorders that are characterized by abnormal bone marrow differentiation and maturation, which leads to bone marrow failure with peripheral cytopenias, dysfunctional blood elements, and probability of leukemic conversion. Most cases occur between the ages of 50 and 90 years. Most cases are sporadic.

The disorders range from clonally derived (refractory) anemias to oligoblastic myelogenous leukemia (refractory anemia with excess blasts). The diseases share a propensity to (1) cytopenias, as a result of inappropriate apoptosis, usually of late-stage marrow precursors, and (2) multilineage dysmorphogenesis of blood cells. Red cells often have striking poikilocytosis, anisocytosis, anisochromia, and basophilic

stippling. The marrow usually contains increased erythroid precursors with dysmorphic features, including nuclear distortions and scanty, poorly hemoglobinized cytoplasm. Ringed sideroblasts are almost a constant feature. Neutrophils have anomalies, including bilobed nuclei and hypogranulated cytoplasm, in association with increased marrow granulocyte precursors. Giant and microcytic platelets, often with abnormal granulation, in the blood are associated with megakaryocytic hyperplasia and atypical lobulation of the nucleus and decreased size of megakaryocytes in the marrow. The bone marrow in MDS is typically hypercellular or normocellular, although hypocellularity may also be detected. It is important to distinguish hypocellular MDS from aplastic anemia because the diagnosis dictates clinical management and prognosis. A critical feature that identifies hypocellular MDS is an associated clonal cytogenetic abnormality (such as deletions in chromosome arms 5q and 7q).

The syndrome primarily affects older women, exhibiting anemia and hypercellular and dysmorphic erythropoiesis with lobulated erythroblast nuclei and hypolobulated micromegakaryocytes but usually normal or elevated platelet counts. It is the most indolent form of the myelodysplastic syndrome with the lowest propensity to evolve into AML. In the more progressive syndromes, leukemic blast cells are

increased, cytopenias are more severe, and the disease has high morbidity and mortality from infection and bleeding. Each of the syndromes has a propensity to evolve into frank AML ranging from approximately 10 to 15 percent in the clonal (refractory) anemias to approximately 40 to 50 percent of patients with trilineage cytopenias and increased marrow blast cells. Mortality from infection is a high risk in patients with severe leucopenia.

Disorders of the hematopoietic system including lymphadenopathy, anemia, leukopenia, and/or thrombocytopenia are common throughout the course of HIV infection and may be the direct result of HIV, manifestations of secondary infections and neoplasms, or side effects of therapy.

Direct histologic examination and culture of lymph node or bone marrow tissue are often diagnostic. A significant percentage of bone marrow aspirates from patients with HIV infection have been reported to contain lymphoid aggregates, the precise significance of which is unknown. Initiation of HAART lead to reversal of most hematologic complications that are the direct result of HIV infection.

CAUSES OF BONE MARROW SUPPRESSION IN PATIENTS WITH HIV INFECTION

HIV infection

Mycobacterial infections

Fungal infections

B19 parvovirus infection

Lymphoma

Medications

Zidovudine

Dapsone

Trimethoprim/sulfamethoxazole

Pyrimethamine

5-Flucytosine

Ganciclovir

Interferon-α

Trimetrexate

Foscarnet.

In patients with SLE apart from antibodies to double strand DNA and anti-smith antibodies, antibodies that target each of the cellular blood elements are also common. Anemia is present in about 50% of patients and is multifactorial. It can be associated with a positive Coombs test or microangiopathic hemolysis or reflect chronic disease (normochromic, normocytic). Leukopenia, particularly lymphopenia, is observed, with the lymphocyte count decreasing in the setting of increased disease activity. Antibodies that bind to lymphocytes and neutrophils have been described, and an increased tendency for lymphocytes to undergo spontaneous apoptosis may contribute to lymphopenia. Idiopathic thrombocytopenic purpura can be an early manifestation of SLE, and thrombocytopenia, induced by antiplatelet antibodies, can sometimes lead to a life-threatening risk for hemorrhage.

Our study attempts to find the common causes and clinical presentation of patients with pancytopenia.

MATERIALS

&

METHODS

MATERIALS AND METHODS

Study Design:

Prospective Cross-Control Study.

Study Population:

Patients admitted to general medical wards at Government General Hospital, Chennai.

Inclusion criteria:

Patients admitted to general medical ward with

- Age > 13 yrs,
- Hb hemoglobin of less than 12 g per dL in women and less than 13 g per dL in men,
- WBC < 4000 cells/µl,
- Platelet count < 1,50,000 /µl.

Exclusion criteria:

- Patients with a known hematological condition
- Patients on cancer chemotherapy
- Patients who received blood transfusion.

Ethical Clearance:

Obtained.

Informed Consent:

Obtained from all patients.

Methodology:

A total of 65 patients were identified over a period of 8months (jan 2010 – aug 2010) according to the above criteria and were included in the study.

In all patients a detailed relevant history was taken including the dietary history, treatment history, alcohol intake,drug intake as well as radiation exposure. Meticulous clinical examination of every patient was done for pallor, fever,bleeding tendencies, jaundice, hepatomegaly, splenomegaly, sternal tenderness, and lymphadenopathy.

Basic investigations were performed for each patient including Haemoglobin, Total leukocyte count, Platelet count, Reticulocyte count and Liver function tests.Absolute values including packed cell volume (PCV), Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated for every patient.Viral markers (HBsAg,Anti HCV,HIV)were done in all patients. Chest radiograph and

abdominal ultrasonography were done all patients. Peripheral smear examination and Bone marrow examination were done in all patients and wherever required, a trephine biopsy was also performed. Vit B12 levels , serum folate levels, upper and lower gastrointestinal endoscopy were done in selected patients.Also thyroid profile is done in selected patients.

Statistical Analysis:

Data analysis was done with use of SPSS, version 13. Descriptive statistics were used to calculate the frequency, mean, and standard deviation. To examine the linear trend of the proportions, trend chi-square was used and to find the test of association chi-square was computed.

Financial support:

Nil

Conflicts of interest:

None

S.NO	Parameter	Method
1.	Complete blood count	Automated flow cytometry
2.	ESR	Westergren method
3.	Urea	GLDH/urease
4.	Creatinine	Picrate method
5.	Serum albumin	Bromocresol green
6.	Serum bilirubin	Calorimetric endpoint diazo
7.	Total protein	Biuret method
8.	Serum Vitamin B12	Electro Chemi Luminescence Immuno Assay
9.	Serum Folate	Electro Chemi Luminescence Immuno Assay
10.	HIV	Enzyme Linked Immunosorbent Assay
11.	HbSAg	Enzyme Linked Immunosorbent Assay
12.	HCV	Enzyme Linked Immunosorbent Assay
13.	Serum T4	Chemi Luminescence Immuno Assay
14.	Serum TSH	Chemi Luminescence Immuno Assay
15.	Occult blood in stools	Standard guiac test
16.	Serum ferritin	Electro Chemi Luminescence Immuno Assay
17.	Serum iron	Ferrozine photometry

NORMAL VALUES

Hemoglobin	M: 13.3 – 16.2gms%	F: 12.0 – 15.8gms%
PCV	M: 38.8 – 46.4	35.4 – 44.4
Total Count	3.54 – 9.06x $10^3/mm^3$	
Platelet Count	165 – 415 x $10^3/mm^3$	
MCV	80 – 100 fL	
MCHC	32.3 – 35.9g/dL	
MCH	26.7 – 31.9 pg/cell	
ESR	M: 0 -15mm/hr	F: 0-20mm/hr
Reticulocyte count	M: 0.8 – 2.3%	F: 0.8 – 2.0 %
Creatinine	M: 0.6 – 1.2mg/dl	F: 0.5 – 0.9mg/dl
BUN	7 – 20 mgs/dl	
Se.Iron	50 – 150µg/dl	
Se.Vitamin B12	279 – 996 pg/ml	
Se.Folate	5.4 – 18.0 ng/ml	
Se.LDH	115-221 IU/L	
Se.TSH	0.3 – 5.5 µIU/ml	
Se.T4	0.7 – 1.8 ng/dl	
Total Bilirubin	0.3 – 1.3 mgs/dl	
Direct Bilirubin	0.1 – 0.4 mgs/dl	
SGOT	12 – 38 U/L	
SGPT	7 – 41U/L	
Se.Alkaline phosphatase	33 – 96 U/L	
Total Protein	6.7 – 8.6 gms/dl	
Se.Albumin	3.5 – 5.5 gms/dl	
Se.Ferritin	M:29-248µg/L F:10-150µg/L	

OBSERVATIONS

&

RESULTS

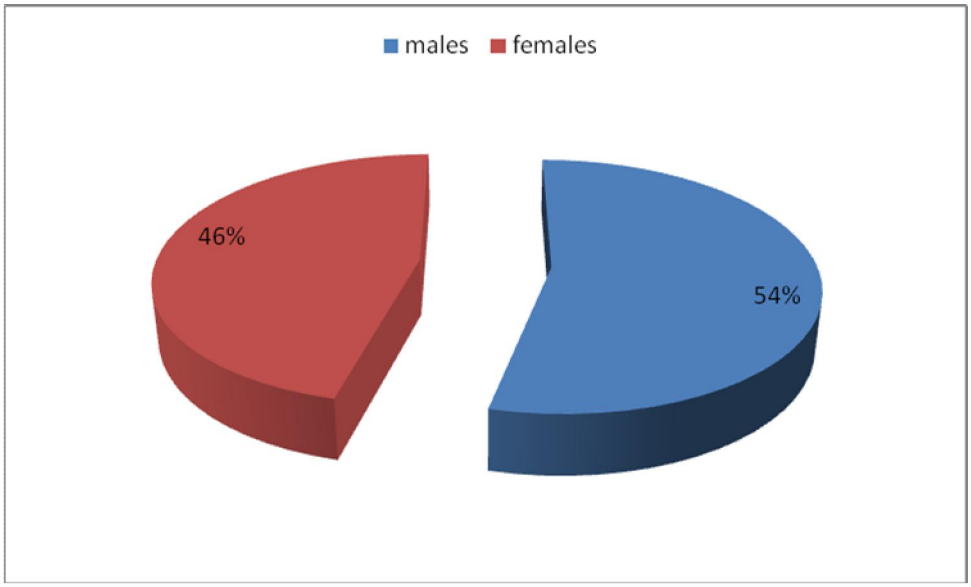
OBSERVATIONS & RESULTS

STUDY POPULATION CHARACTERISTICS:

A total no of 65 patients were found to have pancytopenia between Jan 2010 and Aug 2010.

TABLE:1 SEX DISTRIBUTION			
	NO. OF PATIENTS	**PERCENTAGE**	**p - value**
Males	35	53.85%	0.385
Females	30	46.15%	
Total	65	100.00%	

FIGURE: 1 SEX-WISE DISTRIBUTION OF PATIENTS

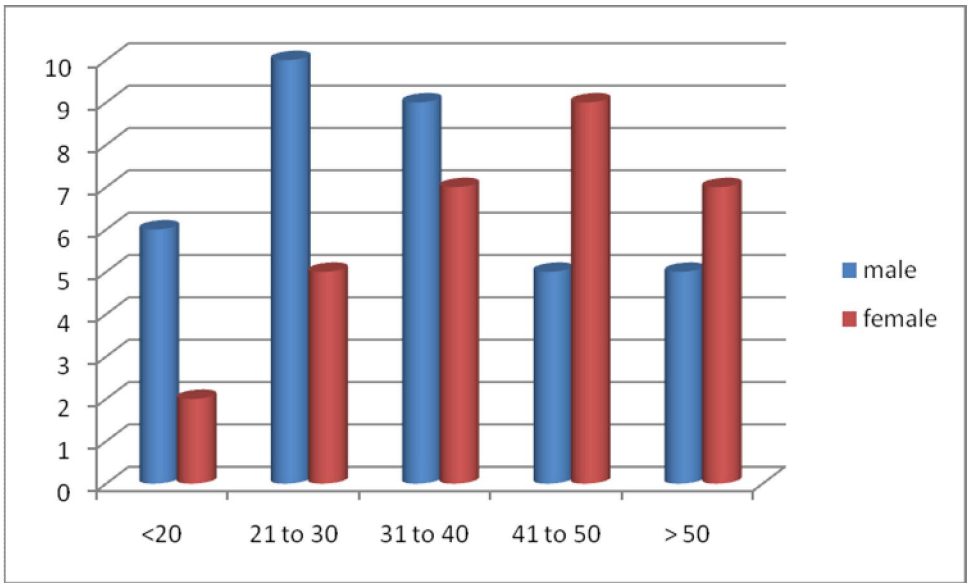


Among 65 patients included in our study, 35 (53.85%) patients were male, and 30 (46.15%) patients were female, though it is not statistically significant with p-value of 0.385.

TABLE:2 AGE AND SEX DISTRIBUTION OF STUDY POPULATION

Age Group	Males	Females	Total	Percentage
Below 20	6	2	8	12.30%
21- 30	10	5	15	23.07%
31 – 40	9	7	16	24.62%
41 – 50	5	9	14	21.54%
Above 50	5	7	12	18.46%
Total	35	30	65	100.00%

FIGURE: 2 DISTRIBUTION OF PATIENTS BASED ON AGE



Male preponderance is seen in patients < 30 yrs of age while female preponderance is seen in age group above 40 yrs of age though this finding is statistically insignificant (p – value of 0.545)

The age of the patients ranged between 14 yrs and 60 yrs with maximum no of patients seen between 31 – 40 yrs of age with a slightly male preponderance.

The Mean age of the patients included in the study is 37.12 mean years, with S.D. of 10.2 years, with mean age of males being 33.51years and females 41.33 years. No of patients were equally distributed among all age groups, though males were more common in younger age group.

CLINICAL PRESENTATION:

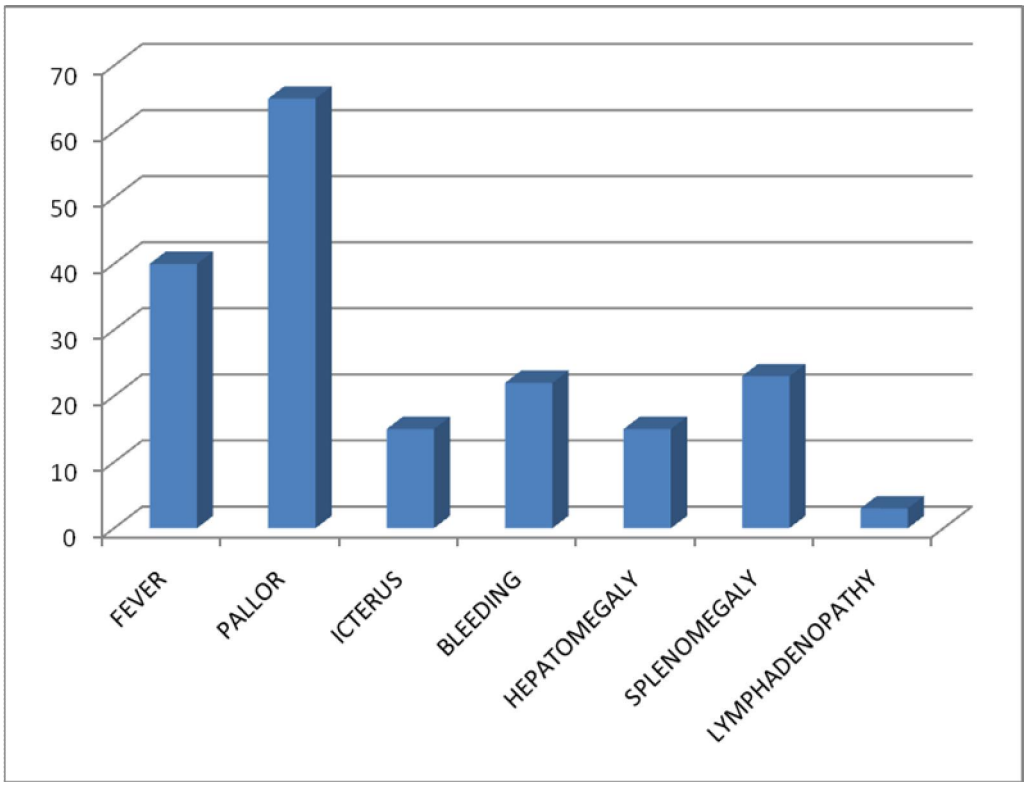
TABLE: 3 CLINICAL FEATURES OF PATIENTS ACCORDING TO VARIOUS ETIOLOGIES

DIAGNOSIS	A	B	C	D	E	F	G
MEGALOBLASTIC ANEMIA	12	25	3	0	7	7	0
APLASTICANEMIA	14	16	2	12	1	1	0
HYPERSPLENISM	2	8	6	4	1	8	0
ACUTE LEUKEMIA	6	6	0	4	4	3	3
MYELODYSPLASTIC SYNDROME	1	4	2	1	0	2	0
MYELOFIBROSIS	0	1	1	1	1	1	0
CONNECTIVE TISSUE DISORDERS	2	2	1	0	0	1	0
HIV RELATED	1	1	0	0	0	0	0
INFECTION INDUCED	2	1	0	0	1	0	0
TOTAL	40	65	15	22	15	23	3

A-FEVER
B-PALLOR
C-ICTERUS
D-BLEEDING
E-HEPATOMEGALY
F-SPLENOMEGALY
G-LYMPHADENOPATHY

Pallor was present in almost all cases. Fever was the second most common presentation in our study as(40 out of 65 patients) 61.54% of patients had fever during the course of illness which is stastically insignificant with a p value of 0.063.

FIG: 3 VARIOUS CLINICAL FEATURES OF PATIENTS WITH PANCYTOPENIA



33.84% of patients (22) had bleeding manifestations, and are found to have either aplastic anemia or acute leukemias which is stastically significant(p vaue 0.009)

Icterus was present in 23.07% of the patients(15).Most of them had chronic liver disease or megaloblastic anemia which is stastically significant(p vaue < 0.001,significant at 5% level).

Liver was palpable in 15 (23.07%) of patients and was predominantly seen in patients with megaloblastic anemia and leukemia which is stastically significant(p vaue < 0.001,significant at 5% level).

Splenomegaly was found in 23 patients (35.38%); found in all cases of hypersplenism, and in few cases of megaloblastic anemia, MDS, and myelofibrosis which is stastically significant(p vaue < 0.018).

Lymphadenopathy was found only in 3 (4.62%) cases and seen in patients with acute leukemia which is stastically significant(p vaue < 0.001,significant at 5% level).

PERIPHERAL SMEAR FINDINGS:

A detailed peripheral smear examination was done in all patients.

TABLE: 4 PERIPHERAL SMEAR FINDINGS ACCORDING TO VARIOUS DIAGNOSIS

DIAGNOSIS	A	B	C	D	E	F	G	H
MEGALOBLASTIC	23	7	23	0	1	6	15	-
APLASTIC ANEMIA	4	-	-	-	-	-	1	9
HYPERSPLENISM	-	-	-	-	-	4	-	8
ACUTE LEUKEMIA	-	-	-	6	-	-	-	1
MDS	1	-	-	-	-	-	-	3
MYELOFIBROSIS	1	-	-	-	-	-	-	1
CTD	-	-	-	-	-	-	-	2
HIV	-	-	-	-	-	-	-	1
VIRAL INFECTION	-	-	-	-	-	-	-	1
TOTAL	29	**7**	23	6	1	10	16	26

A - Anisopoikilocytosis

B - Erythroblasts

C - Hypersegmented neutrophils

D - Immature WBC

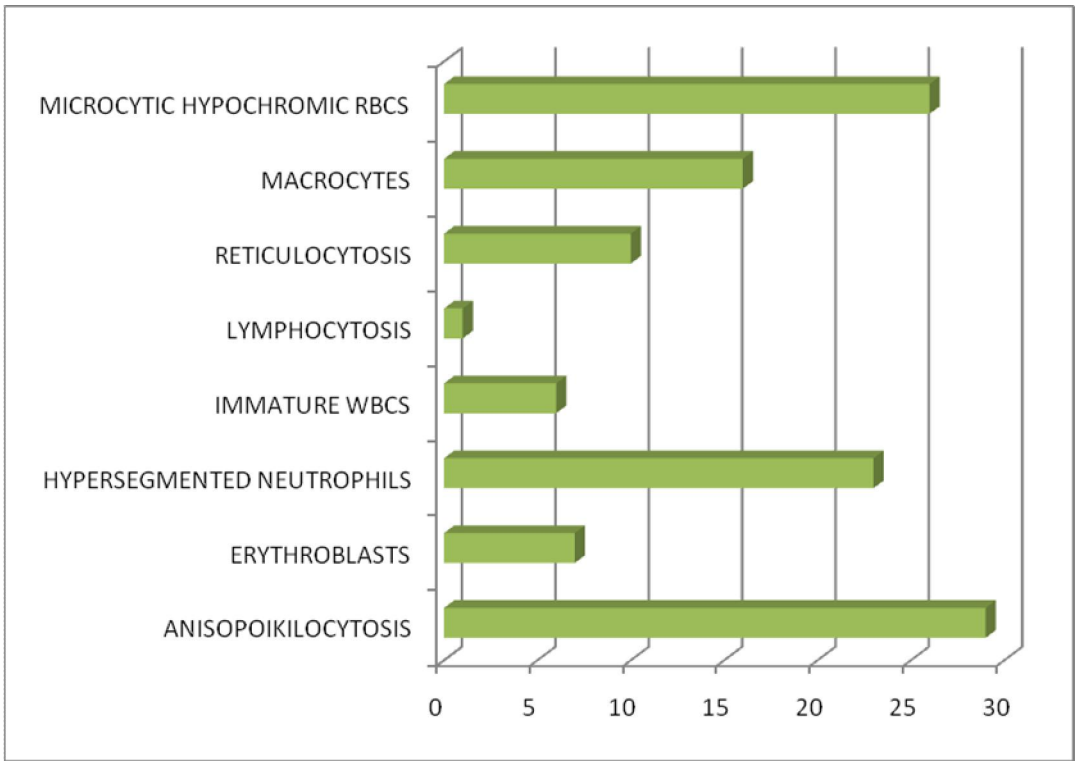
E – Lymphocytosis.

F – Reticulocytosis

G- Macrocytes

H-Microcytic,hypochromic RBCs

FIG:4 PERIPHERAL SMEAR FINDINGS IN PATIENTS WITH PANCYTOPENIA



Anisopoikilocytosis and Hypersegmented neutrophils were the predominant finding (92%) in cases of megaloblastic anemia; other findings being erythroblasts, lymphocytosis, and reticulocytosis.

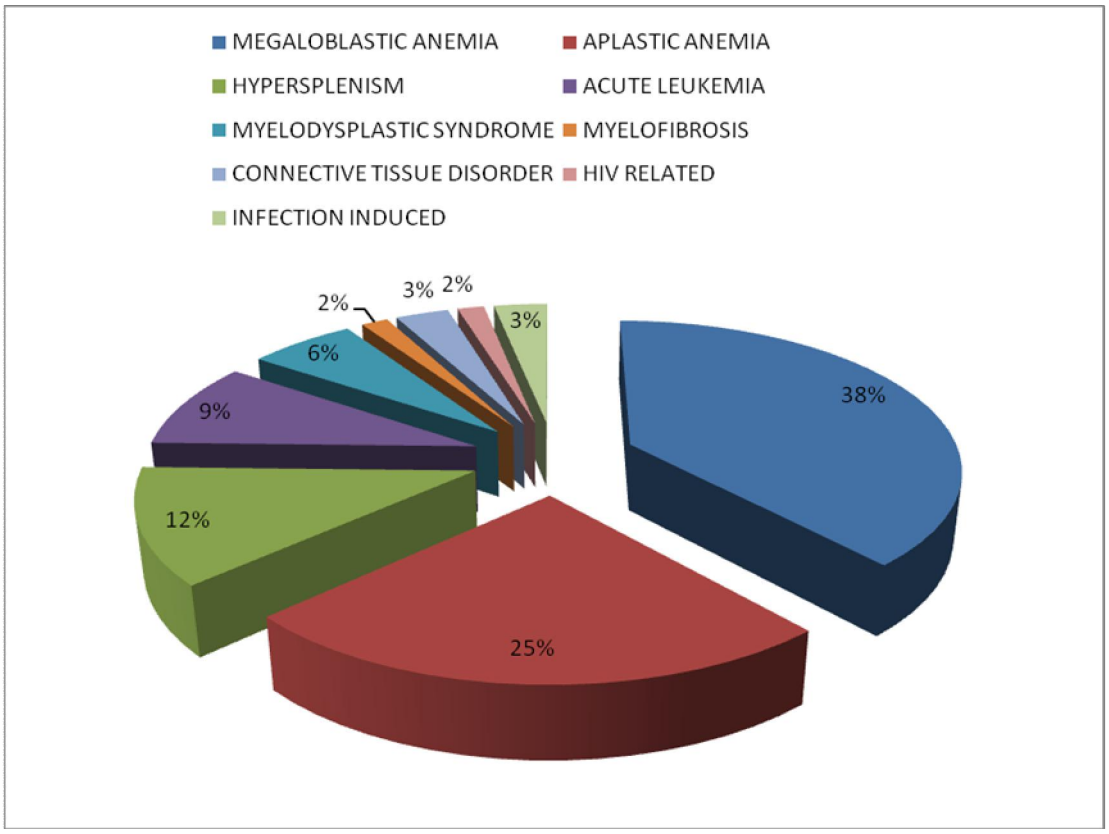
Anisopoikilocytosis was also found in few cases of aplastic anemia. Peripheral blood WBC blasts were found in 4 cases of acute leukemia and in a case of MDS.

Atypical lymphocytes were found in two cases of viral infection.

Pseudo Pelger Huet cells (hyposegmented neutrophils) were present in two cases of myelodysplastic syndrome.

VARIOUS ETIOLOGIES OF PANCYTOPENIA:

FIGURE: 5 DISTRIBUTION OF VARIOUS ETIOLOGIES OF PANCYTOPENIA

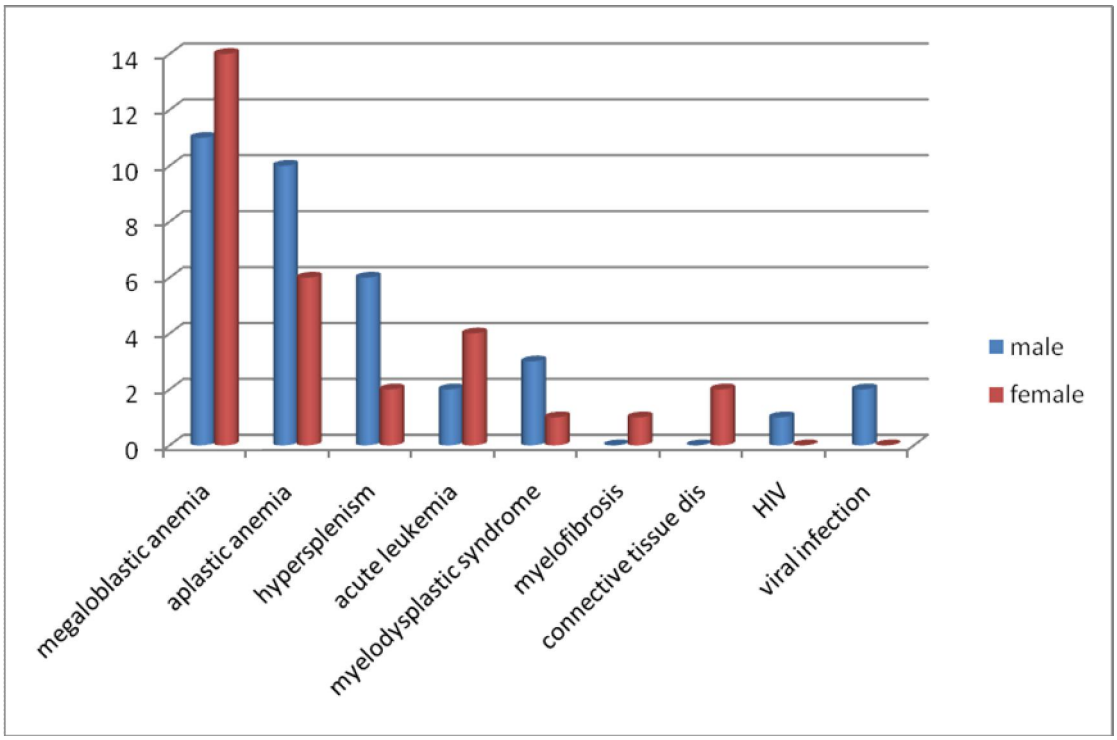


The most common cause of pancytopenia in our study was megaloblastic anemia (38.46%), followed by aplastic anemia (24.62%), hypersplenism (12.31%). The other causes are acute leukemias (9.23%), Myelodysplastic syndrome (6.15%), collagen vascular disorder (3.08%), viral infection (3.08%), HIV (1.54%), and myelofibrosis (1.54%).

TABLE: 5 DISTRIBUTION OF CAUSES OF PANCYTOPENIA ACCORDING TO SEX

DIAGNOSIS	MALE	FEMALE	TOTAL
MEGALOBLASTIC ANEMIA	11	14	25 (38.46%)
APLASTIC ANEMIA	10	6	16 (24.62%)
HYPERSPLENISM	6	2	8 (12.31%)
ACUTE LEUKEMIA	2	4	6 (9.23%)
MYELODYSPLASTIC SYNDROME	3	1	4 (6.15%)
MYELOFIBROSIS	0	1	1 (1.54%)
CONNECTIVE TISSUE DISORDER	0	2	2 (3.08%)
HIV INFECTION	1	0	1 (1.54%)
VIRAL INFECTION	2	0	2 (3.08%)
TOTAL	35	30	65

FIGURE: 6 DISTRIBUTION OF CAUSES OF PANCYTOPENIA ACCORDING TO SEX



Megaloblastic anemia was more common in females (14) compared to males (11) in our study. While Aplastic anemia is common in males (10) than females (6); both of which are statistically significant.

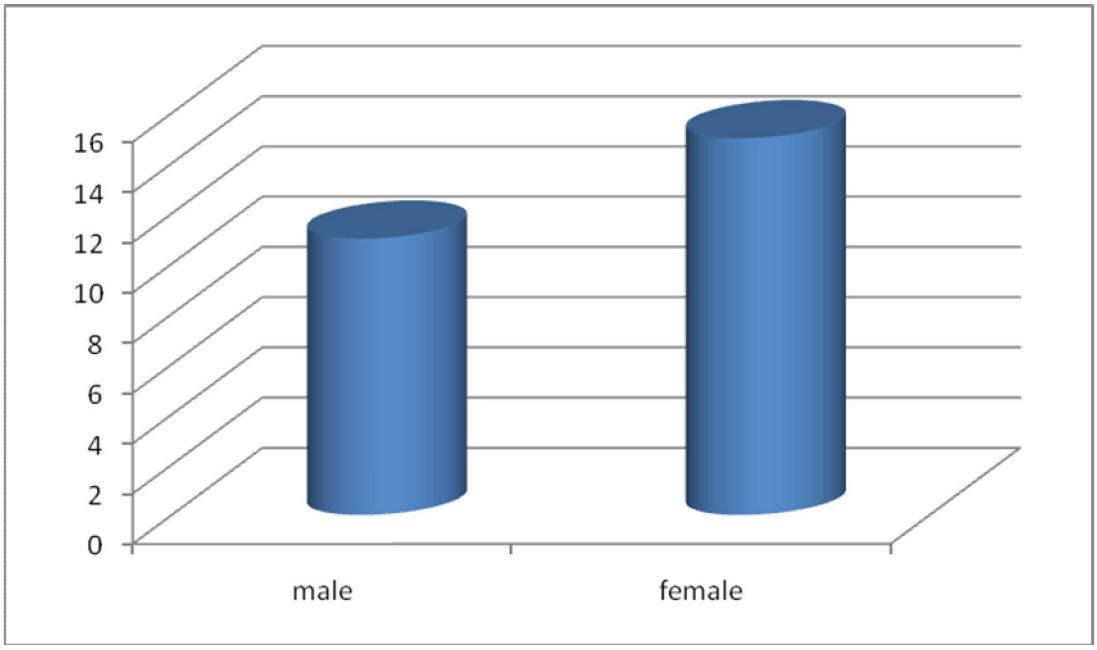
Hypersplenism, MDS, viral infections were common in males; while acute leukemias, myelofibrosis were common in females.

MEGALOBLASTIC ANEMIA:

Mean age of patients with megaloblastic anemia is 39.32 yrs.

84 % of patients had macrocytosis; with a maximum of 127.3femtolitres; 16% of patients had normocytic anemia.

FIGURE 7: DISTRIBUTION OF MEGALOBLASTIC ANEMIA ACCORDING TO SEX



56% of patients (14) with megaloblastic anemia are females, and the remaining 44% are males (11).

84% of patients with megaloblastic anemia had MCV > 100 femtolitres; and 16% of them had MCV in normal range < 100 femtolitres.

FIGURE 8: DISTRIBUTION OF PATIENTS ACCORDING TO MCV

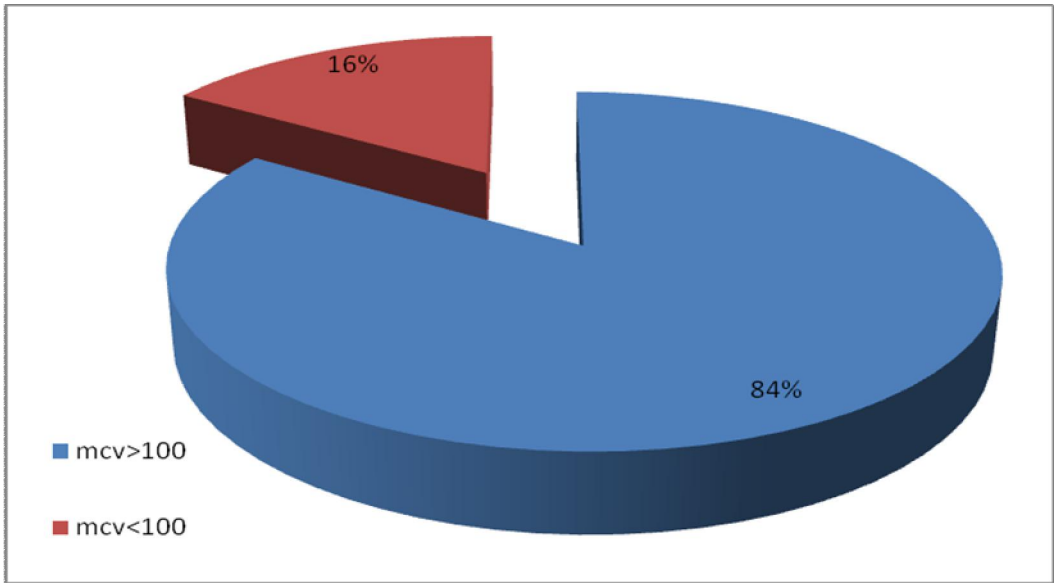
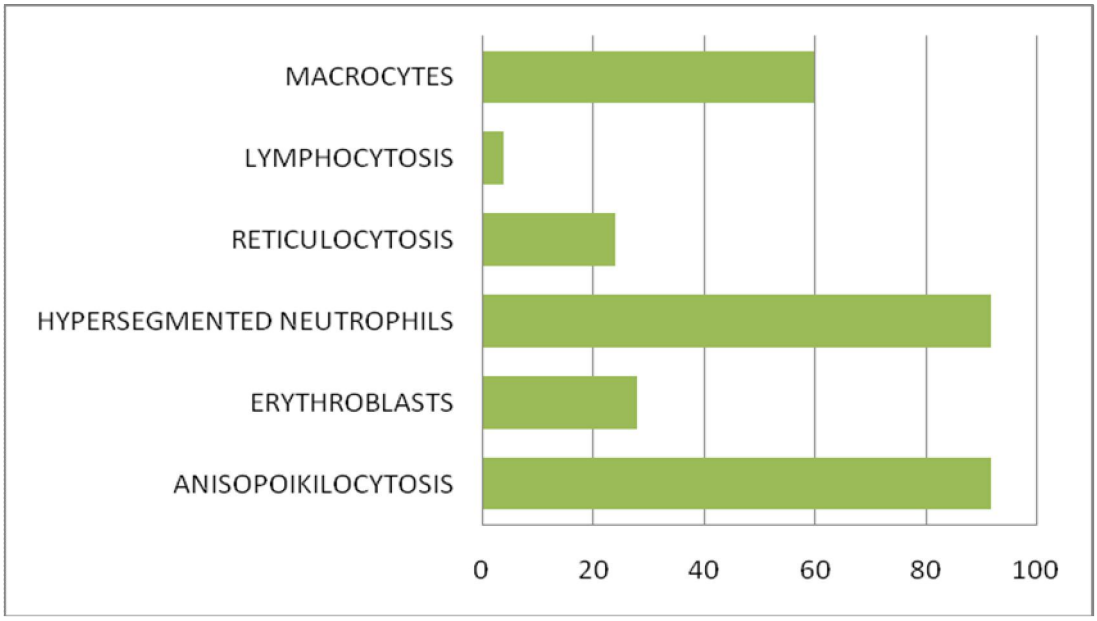
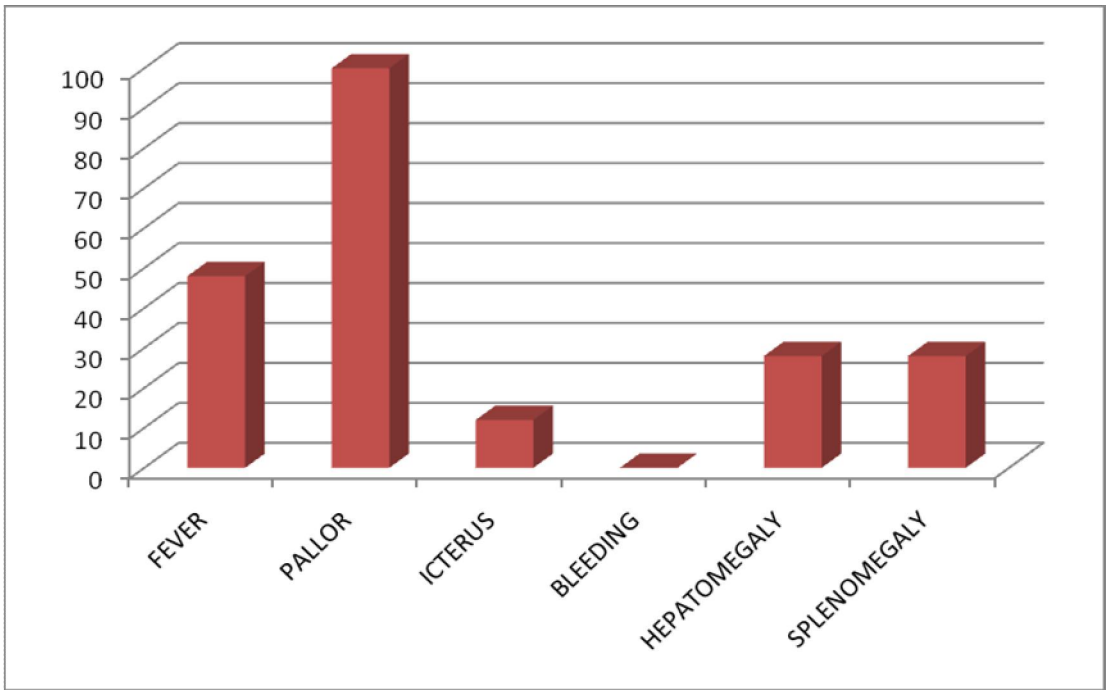


FIGURE 9: PERIPHERAL SMEAR FINDINGS IN PATIENTS WITH MEGALOBLASTIC ANEMIA



Anisopoikilocytosis (92%), and hypersegmented neutrophils (92%) are the most common findings in peripheral smear of patients with megaloblastic anemia.

FIGURE 10: CLINICAL FEATURES OF PATIENTS WITH MEGALOBLASTIC ANEMIA



Pallor was present in all cases. The other features were fever (48%), icterus (12%), hepatomegaly (28%), and splenomegaly (28%).

21 patients had vitamin B12 deficiency and 4 had folate deficiency.Among the 11 male patients with Megaloblastic anemia 7 were alcoholics,2 patients had abdominal surgeries,one patient had

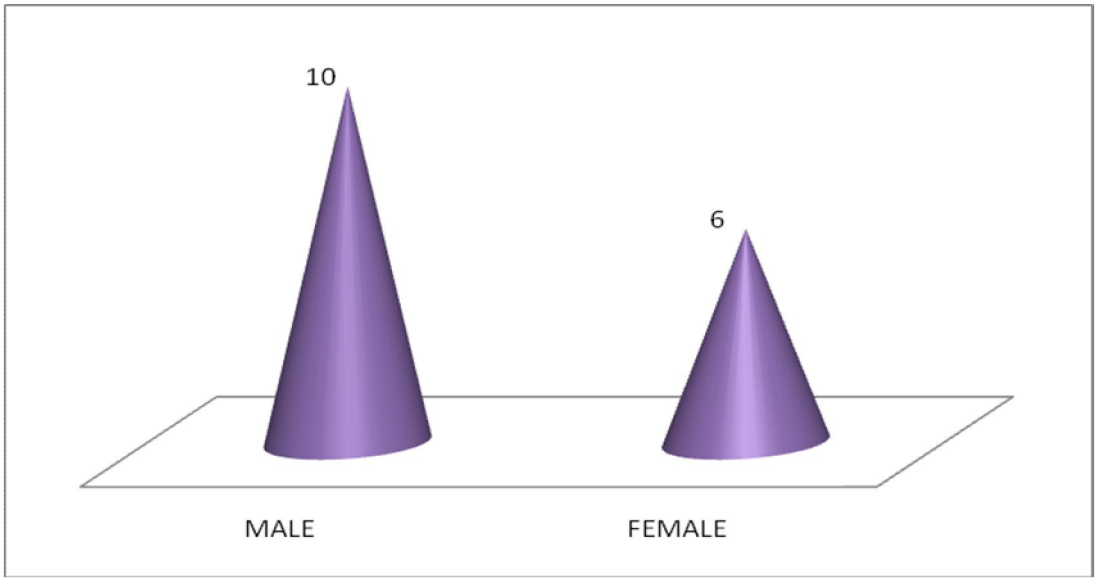
features of malabsorption and another one was a pure vegetarian.Among 14 female patients with Megaloblastic anemia 4 were diagnosed to have hypothyroidism,2 patients had pernicious anemia.3 female patients were pure vegeterians.another 2 patients had history of consumption of anti epileptic drugs.

APLASTIC ANEMIA:

24.62% of patients had aplastic anemia. Of which 10(62.5%) were male and 6(37.5%) were female.Mean age of patients with aplastic anemia is 33.43 yrs.Average Hb% of these patients is 4.80 gms%.

56.25% of patients had thrombocytopenia < 10,000 cells/cumm.

FIGURE 11: DISTRIBUTION OF APLASTIC ANEMIA ACCORDING TO SEX



68.75% of patients with aplastic anemia had MCV<100 femtolitres while 31.25% had MCV>100 femtolitres.

FIGURE 12: DISTRIBUTION OF PATIENTS WITH APLASTIC ANEMIA ACCORDING TO MCV

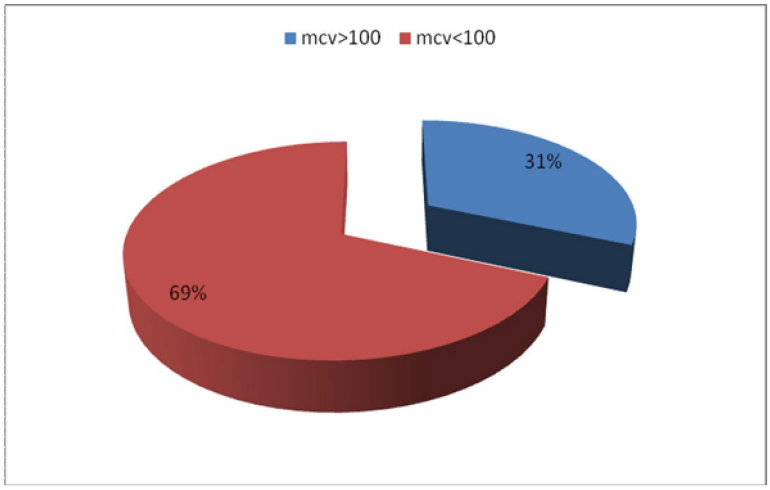
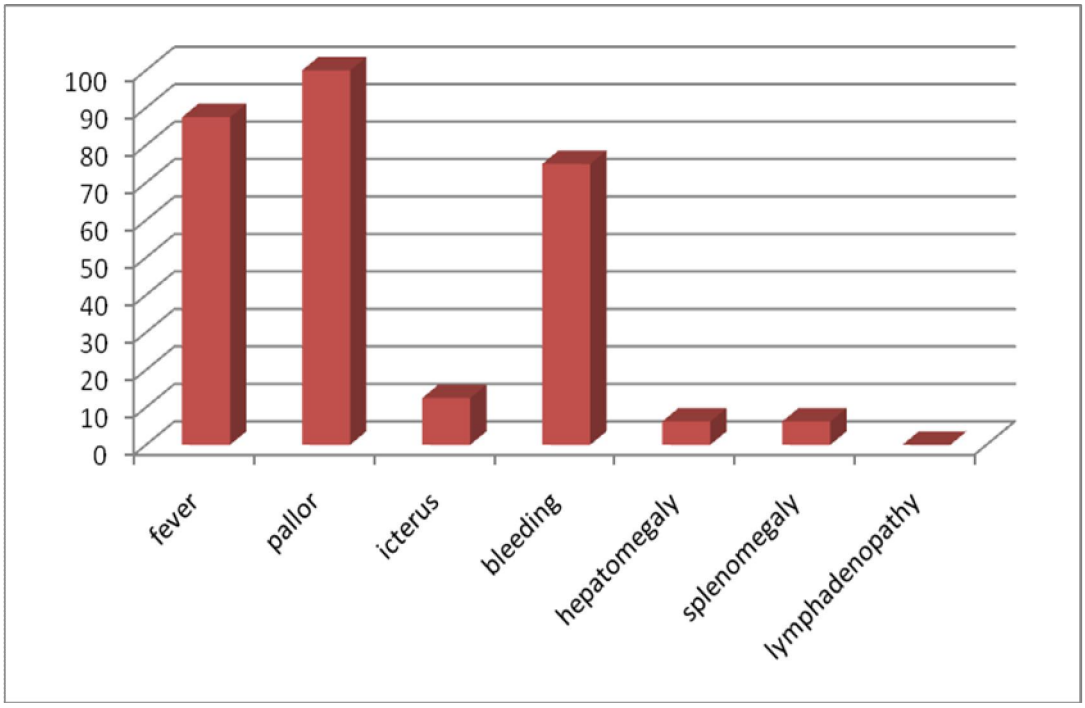


FIGURE 13: CLINICAL FEATURES OF PATIENTs WITH APLASTIC ANEMIA



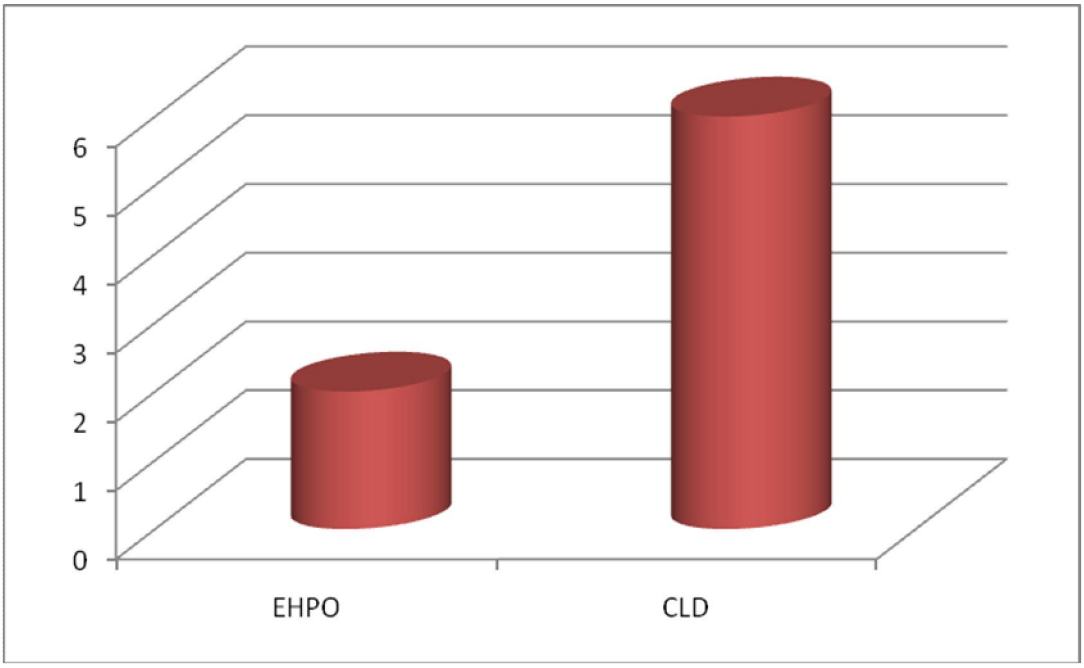
The various clinical features of patients with aplastic anemia were pallor (100%), fever (87.5%), icterus (12.5%), bleeding (75%), hepatomegaly (6.25%), and splenomegaly (6.25%).

HYPERSPLENISM

8 patients (12.31%) with pancytopenia were diagnosed to have hypersplenism of which 6 were male and 2 were female patients.

Out of 8 patients 2(25%) had Extra Hepatic Portal Obstruction, while the remaining 6 (75%) had Cirrhosis of liver leading to hypersplenism.

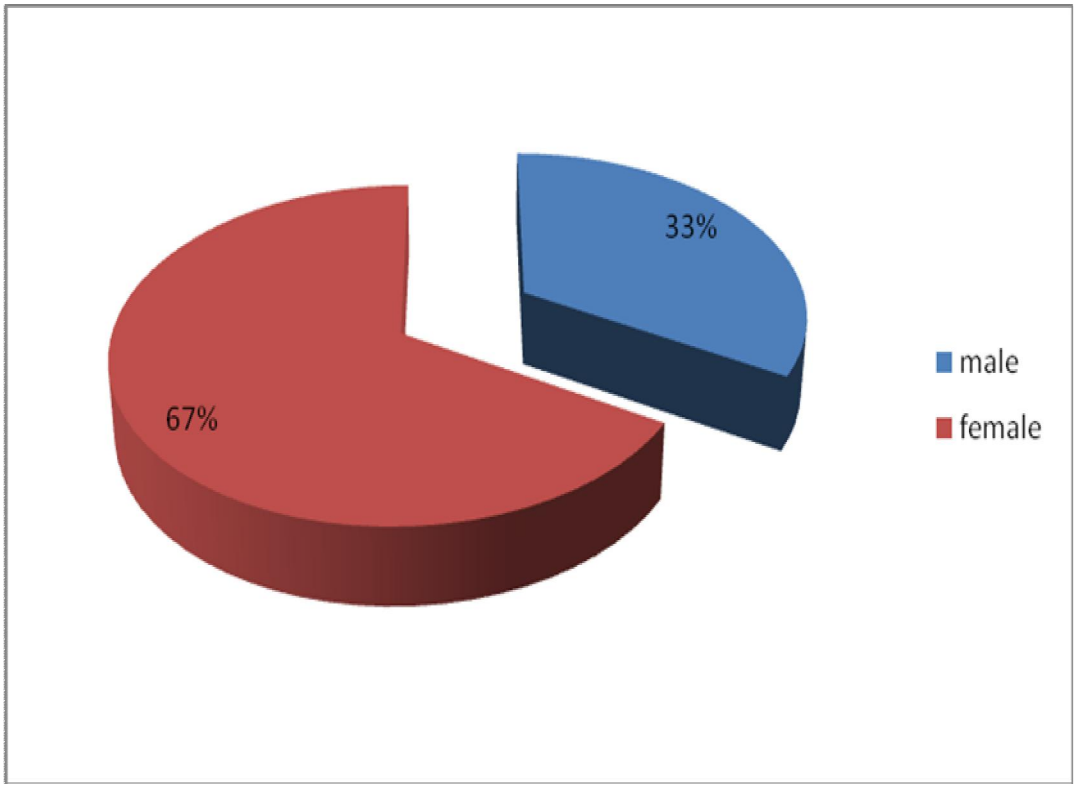
FIGURE 14: VARIOUS ETIOLOGIES OF HYPERSPLENISM



ACUTE LEUKEMIA

6 patients (9.23%) was diagnosed to have acute leukemias; 4(66.7%) of them with acute myeloid leukemia; 2(33.3%) with acute lymphoid leukemia.out of the 6 patients 2 were males and 4 were females.

FIG:15 DISTRIBUTION OF PATIENTS WITH LEUKEMIA ACCORDING TO SEX



All of the patients with leukemia had blasts in their peripheral smear.One of the patients had AML M1 type of leukemia.

MYELODYSPLASTIC SYNDROME

MDS was diagnosed in 4 patients (6.15%); of which 3(75%) were male, and 1 (25%) was female.

Mean age of these patients is 56.25yrs .Pseudo Pelger Huet cells(Hyposegmented neutrophils) were present in two cases of MDS.

Erythroblasts were found in peripheral smear of one of these patients.

MYELOFIBROSIS

One (1.54%) female patient was diagnosed to have myelofibrosis.

VIRAL INFECTIONS

2 patients (3.08%) had features of systemic viral infection; their peripheral smear showed atypical lymphocytes but no blasts.

1 (1.54%) male patient was positive for HIV.

COLLAGEN VASCULAR DISORDER

2 patients (3.08%) were found to have Systemic lupus erythematosis; both of them were young females.

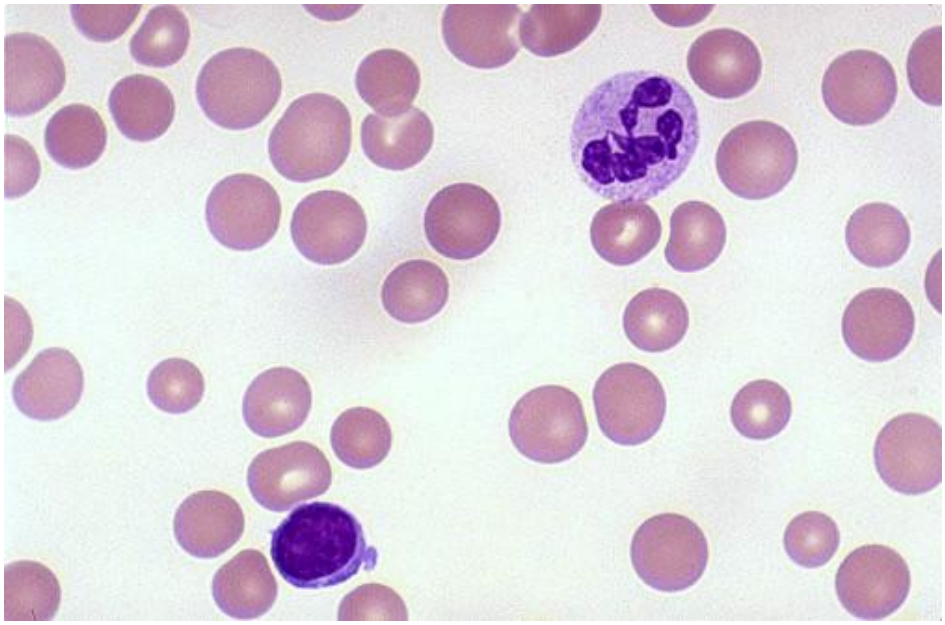


Fig: 1 peripheral smear of a patient with megaloblastic anemia showing anisopoikilocytosis with hypersegmented neutrophil.

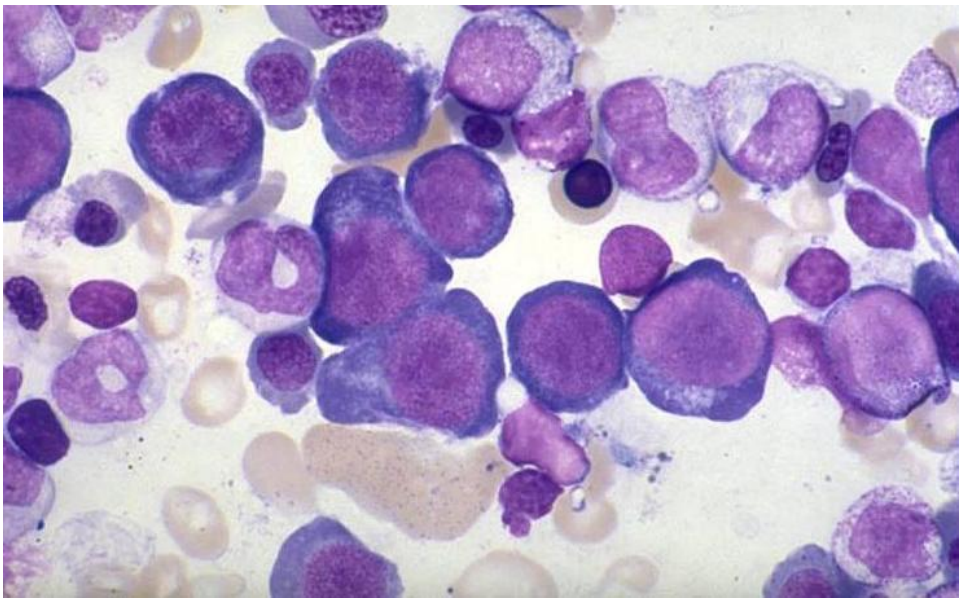


Fig: 2 Bone marrow examination of a patient with megaloblstic anemia showing hypercellular with increased erythropoiesis, larger megakaryocytes with hyperlobated nuclei

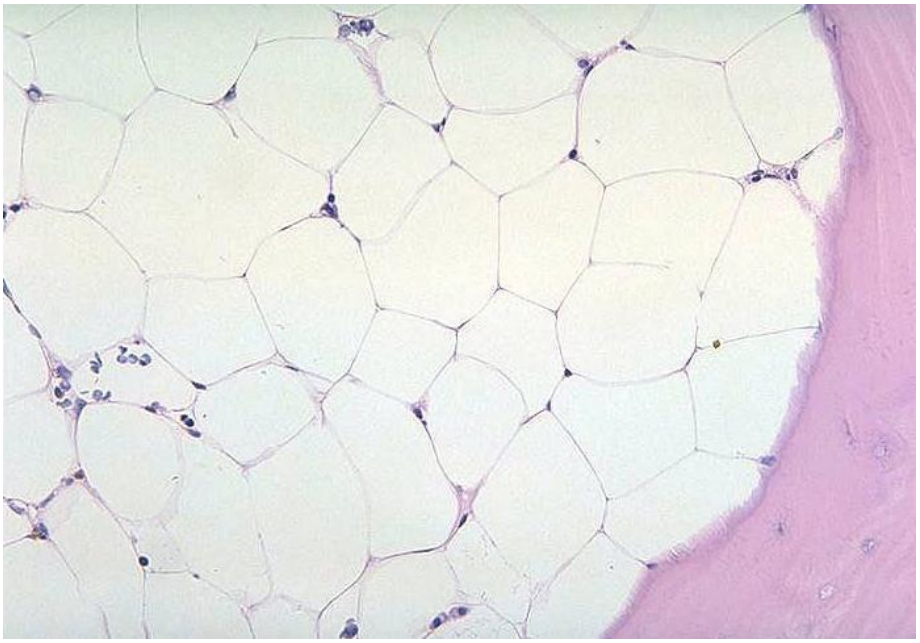


Fig: 3 Bone marrow examination of a patient with aplastic anemia showing hypocellular marrow replaced by fat.

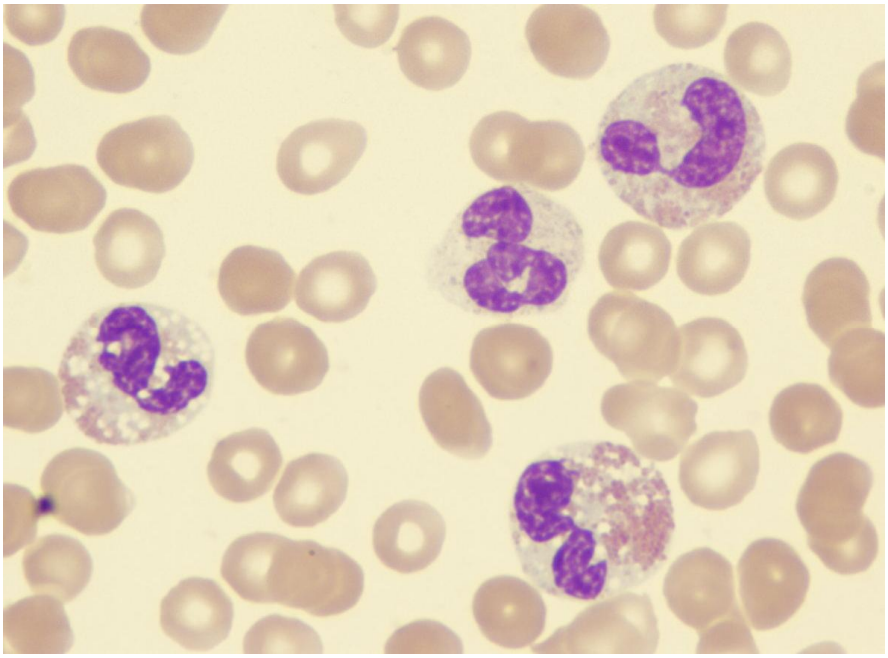


Fig: 4 Blood smear of a patient with Myelodysplastic Syndrome showing hypogranulated eosinophils with hyposegmented nuclei.(Pseudo Pelger huet cells).

DISCUSSION

DISCUSSION

Pancytopenia is a serious hematological problem which presents with anemia, bleeding manifestations and infections. There are only a limited number of studies from India on the frequency of various causes of pancytopenia.The variation in the frequency of various entities causing pancytopenia has been attributed to the differences in methodology and stringency of diagnostic criteria, geographic area, period of observation,genetic differences and exposure to various myelotoxic agents. Our study included 65 patients and the age group of the patients range from 14 to 60 years. Of these 30 were females and 35 were males. The mean age of the patients is 37.12 years. Most male patients are under 30 years and females more than 40 years.

Analysis of the data observed in our study has shown the etiology distribution of pancytopenia to be Megaloblastic anemia(25 cases; 38.46%), Aplastic anemia(16cases;24.62%),Hypersplenism(8 cases;12.31%),Acute leukemias(6 cases;9.23%),Myelodysplastic syndrome(4 cases;6.15%),Myelofibrosis(1 case;1.54%),Connective tissue disorder(2 cases;3.08%)HIV infection(1 case;1.54%)and Viral infection(2 cases;3.08%).

Incidence of Megaloblastic anemia varies from 0.8 to 32.26% in various studies. In our study the incidence of Megaloblastic anemia is 38.46%. Similar results were obtained in the studies done by Kumar et al[1](22%) , Aziz et al[2] (40.9%) , Savage et al [3],Iqbal et al[7] . However the study by Tilak et al[4] showed the incidence to be 68%.

In our study, the predominant signs present in patients with megaloblastic anemia were pallor(100%) followed by fever(48%), hepatomegaly(28%), splenomegaly(28%) and icterus(12%).Similar results were shown in the studies done by Tilak et al[4] ,Khunger et al[5](pallor in 100% of patients with Megaloblastic anemia)and Aziz et al[2](pallor in 98% of patients with megaloblastic anemia).

In our study, 92% of Megaloblastic anemia patients had hypersegmented neutrophils in their peripheral smear and 28% had circulating megaloblasts.This is in concordance with the studies done by Tilak et al[4],Khunger et al[5]and Ishtiaq et al[15].

Most of the megaloblastic anemia in our study were due to Vitamin B12 deficiency (84%).16% were due to folate deficiency.Similar results were shown in the study done by Aziz et al[2](77.77% of patients had Vit B12 deficiency and33.33% had folate deficiency).

In our study,84% of patients with megaloblastic anemia had MCV more than 100fl.16% had MCV less than 100 fl. The maximum MCV noted was 127.3 fl.Megaloblastic anemia should be considered on top if MCV is greater than 100 fl.Most of the patients had increased levels of serum iron and ferritin.Most of the precursor cells are destroyed in the marrow due to ineffective erythropoiesis and therefore serum iron is not utilized.Once treatment is started with Vit B12 or folate the serum iron and ferritin levels fall.

Bone marrow aspiration showed typical megaloblasts with sieved chromatin and asynchronic nuclear cytoplasmic ratio.Though we have done bone marrow aspiration for all patients it can be deferred in those cases presenting with hepatosplenomegaly and having hypersegmented neutrophils and or circulating megaloblasts in their peripheral smear.These patients can be put on a trial of hematinics with a close hematologic follow up.

Megaloblastic anemia was present in all age groups.Among the 11 male patients with megaloblastic anemia in our study 7 were chronic alcoholics and 2 patients had undergone abdominal surgeries(one patient underwent surgery for peptic ulcer disease and another one ileal

resection).One patient had loose stools along with loss of weight for more than three months.Upper GI endoscopy showed erosions in the stomach and Lower GI endoscopy revealed cryptitis with cryptic abscess suggestive of Ulcerative colitis.One male patient was a pure vegetarian with even no milk consumption.

In our study, there were 14 females with megaloblastic anemia.Among them 4 patients were diagnosed to have hypothyroidism.Most of them were above 50 years.One young female presented with jaundice,anemia and fever.she was diagnosed to have Vit B12 deficiency with features of hemolysis.2 female patients had atrophic gastritis in upper GI scopy suggestive of Pernicious anemia confirmed by histopathological examination.Of these two patients one had arthralgias,myalgias and history suggestive of skin rashes.The other patient had family history of similar illness. 3 female patients with megaloblastic anemia were pure vegeterians. In two patients with megaloblastic anemia there is a general decrease in the intake of food due to poverty. The higher prevalence of nutritional deficiency has been cited for the increased frequency of megaloblastic anemia.2 patients had history of consumption of antiepileptic drugs for a longer period with no concomitant folate supplementation.

The incidence of Aplastic anemia varies from 10% to 52.7% in patients with pancytopenia in various studies. In our study the incidence of Aplastic anemia is 24.61%.The mean age of the patients is 33.43 years.The incidence was more common in males(62.5%) as compared to females(37.5%).The most common presentation was pallor(100%) followed by fever(87.5%) and bleeding(75%).One of the patients with Aplastic anemia in our study had splenomegaly.This could be due to the repeated blood transfusions. It is the second most common cause of pancytopenia in our study as shown by Aziz et al[2](31.88%) , Savage et al[3], Khunger et al[5](14%) .The study done by Kumar et al[1] showed aplastic anemia to be the most common cause of pancytopenia with 29.5%.

In Aplastic anemia hematopoiesis fails. Blood cell counts are extremely low and the bone marrow appears empty. 31.25% of patients with Aplastic anemia had MCV more than 100 fl. 56.25% of patients had MCV less than 100 fl . The platelet count was less than 10,000 in 56.25% of patients.

Pathophysiology appears to be immune mediated. Aberrant immune response may be triggered by environmental exposures to chemicals,drugs,viral infections and endogenous antigens.Aplastic anemia is more common in developing countries which may be attributed

to the increased exposure to the toxic chemicals and increased availability of over the counter medications.

Hypersplenism is the third most common cause (12.3%) of pancytopenia in our study. Most of them are males. The study by Aziz et al[2] showed the incidence of hypersplenism in pancytopenic patients to be 6.81% .In our study, 25% of hypersplenism were due to Extra hepatic portal vein obstruction and 75% were due to chronic liver disease. One of the patients with chronic liver disease was hepatitis C positive . The bone marrow of this patient showed adequate hematopoiesis with mild to moderate megaloblastic changes. This ruled out the possibility of Hepatitis C induced myelosuppression.One of the patients was Hepatitis B positive.

In our study,Chronic liver disease is the most common cause associated with hypersplenism followed by extrahepatic portal vein obstruction. This is in contrast to earlier studies done by Jitendar et al[6] , Mohan et al[7] where they found Chronic Malaria and Kala azar to be the predominant causes of hypersplenism. Since those studies were done more than a decade ago the better diagnosis and treatment of Malaria and Kala azar might have lead to the decreased incidence of these diseases in our study.

Acute leukemia was found to be the fourth most common cause (9.23%) of Pancytopenia in our study which is similar to a study conducted by Savage et al[3] who observed that the most common cause of pancytopenia was megaloblastic anemia followed by aplastic anemia, acute leukemia,

AIDS and hypersplenism, and another study by Kumar et al[1] who reported the causes of pancytopenia in order of frequency as Aplastic Anemia at 29.5%, megaloblastic anemia at 22%, Aleukemic Leukemia or lymphoma (18%) and hypersplenism at 11.4%.

Of the 6 patients with acute leukemias, 4 had acute myeloid leukemia, and 2 had acute lymphocytic leukemia.

The incidence of myelodysplastic syndrome is 6.15% in our study . Most of the patients are above 50 years . It is a disease characterized by ineffective hematopoiesis . It differs from AML by its increased apoptosis in early stages. Hyposegmented neutrophils(Pseudo Pelger Huet cells) were seen in the peripheral smear of two patients with MDS. Hypercellularity of bone marrow with abnormal cells confirmed the diagnosis.In all the above patients malignancy,monoclonal gammopathies were ruled out by appropriate investigations.Serum folate and vit B12 levels were normal in all the patients with MDS in our study.

The incidence of connective tissue disorder as a cause of pancytopenia is 3.07%. One of the patients had autoimmune myelofibrosis with autoimmune thyroiditis.

Myelofibrosis was diagnosed in one patient(1.54%) with pancytopenia. There was an extensive marrow replacement by fibrosis. There will be increasing splenomegaly and hepatomegaly due to extramedullary hematopoiesis .The peripheral blood cells are low due to decreased production from the marrow as well as due to hyperfunctioning of the spleen.

One middle aged patient was diagnosed as having HIV induced pancytopenia. But the incidence is low in our study compared to other studies where the incidence ranges from 6 to 10%.This patient was first diagnosed as having HIV in our centre and he was not on any drugs prior to admission.His HCV status was negative and he had no evidence of any lymphoproliferative disorder,tuberculosis or other viral infections.Since all the causes were ruled out the patient was diagnosed to have HIV induced pancytopenia.The bone marrow aspirate in this patient was hypocellular,occasional megakaryocyte with bare nuclei seen.There was a moderate reduction in erythroid progenitors with dyserythropoiesis,mild to moderate reduction in granulocyte progenitors with normal maturation,

Lymphocytes 22%,transformed lymphocytes present,increased Reticuloendothelial cells with hemophagocytosis.

2 of our patients presented with systemic viral infection were found to have pancytopenia. They also had atypical lymphocytes in their peripheral smear. This entity should be considered in patients in whom other causes of pancytopenia has been ruled out and having signs of viral infection.

LIMITATIONS OF THE STUDY

- The major limitation of our study is the small number of subjects we have included in our study.

- Antibodies to Intrinsic factor was not done in pernicious anemia causing Megaloblastic anemia.

- Trephine biopsy evaluation was not done in all patients.Therefore more definitive evaluation of cellularity and exclusion of focal lesions could not be done.

- There has been a very limited follow up of patients and therefore response to therapy could not be assessed.

CONCLUSION

CONCLUSION

- Megaloblastic anemia is the most common cause of pancytopenia in our setting.
- This probably indicates the poor nutritional status of the general population in our community.
- All patients with pancytopenia should be sought for megaloblastic anemia as it is a potentially treatable condition.
- Physicians should have a high index of suspicion for Vitamin B12 deficiency when dealing with patients presenting with symptoms of anemia such as pallor and weakness and/or diagnosed with pancytopenia on further workup.
- The finding of hypersegmented neutrophils in the peripheral smear will guide in the diagnosis of megaloblastic anemia.
- Bone marrow aspiration can be deferred in those cases presenting with hepatosplenomegaly and having hypersegmented neutrophils and or circulating megaloblasts in their peripheral smear.These patients can be put on a trial of hematinics(Vit B12/folate) with a close hematologic follow up.

- Aplastic anemia is the second most common cause of pancytopenia in our study.
- The blood counts were extremely low in patients with aplastic anemia.
- Hypersplenism is an important cause of pancytopenia in our setting.
- Hypersplenism should be sought as a cause of pancytopenia in patients with chronic liver disease especially alcoholics.
- Myelodysplastic syndrome is a common cause of pancytopenia in the elderly population.
- After the common causes have been ruled out patient should be evaluated for rare causes like HIV infection, systemic viral infection, connective tissue disorders, and myelofibrosis.
- Peripheral smear and bone marrow examination would help in identifying the etiology of pancytopenia in almost all patients.
- A Comprehensive evaluation of pancytopenia with a clinico laboratory correlation would help in the appropriate management of potentially treatable conditions.

RECOMMENDATIONS

- Bone marrow aspiration can be deferred in those cases presenting with hepatosplenomegaly and having hypersegmented neutrophils and or circulating megaloblasts in their peripheral smear.These patients can be put on a trial of hematinics(Vit B12/folate) with a close hematologic follow up.

- After ruling out the common diseases causing pancytopenia patients should be investigated for less common conditions like connective tissue disorders etc.

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ANNEXURES

A STUDY ON THE CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH PANCYTOPENIA

PROFORMA

Name: Age: Sex: OP.NO:

Address: Ph.No:

Presenting Complaints:

Easy fatiguability: Fever/chills & rigor:

Dyspnoea: Giddiness:

Jaundice: Abdominal distension:

Lymphadenopathy:

Purpura/Skin rash: Pedal edema:

Loss of Wt: Loss of Appetite:

Night Sweats: Bone Pain:

Bleeding Tendency: Gum bleed/Hematamesis/ Malena/Bleeding PR

Purpura/ Skin rash:

Cough/ burning micturition/loose stools:

Drug intake:

Alcohol intake/smoking:

Co-morbid Illness: DM: HT: TB: Cardiac illness: any malignancy:

Menstrual h/o: undue bleeding PV:

h/o previous treatment/ surgery:

others if any:

EXAMINATION:

Fever:

Pallor: Jaundice:
Lymphadenopathy: Cyanosis:
Clubbing: Pedal edema:
Purpura/Petechiae/Ecchymosis:

Sternal tenderness: Others:

CVS:

RS:

Abdomen:

Genitals:

Per rectal / pelvic examination:

INVESTIGATIONS FOR ALL PATIENTS*:*

CBC

HB%: PCV: ESR:

Reticulocyte Index:

TC: P: L: E: B: M:

Platelets:

Occult Blood in Stools:

Blood sugar:

RFT: Urea: Creatinine:

LFT: Tot.bilirubin: Direct: SGOT: SGPT:
Alkaline phosphatase:

Total Protein: Serum Albumin:

Serum LDH:

ELISA for HIV:

HBsAg: Anti-HCV:

X-RAY CHEST:

ECG:

USG-Abdomen:

Serum B12 level:

Serum Folate:

PT: INR: aPTT:

Peripheral Smear Study:

Bone Marrow Study:

Upper GI scopy:

Lower GI scopy

Serum Electroporesis:

Se.Ferritin:

Others:

FINAL DIAGNOSIS:

MASTER CHART

S.NO	AGE	SEX	FEVER	PALLOR	ICTERUS	BLEED	WT LOSS	ANOREXIA	LIVER	SPLEEN	LYMPHNODES	DYSPNEA	ALCOHOL	FOOD HABITS	SURGERY	HB	PCV	TC	DC	PLATELET	MCV	MCH	MCHC	RPI
1	17	F	YES	YES	YES	NO	NO	NO	NO	NO	NO	YES	NO	MIXED DIET	NO	2.8	9	800	P74L23E3	5000	125	33.4	34.2	2.60%
2	48	M	YES	YES	NO	NO	NO	YES	NO	NO	NO	YES	NO	MIXED DIET	YES	4.8	14	2500	P55L36M9	44000	93.9	32.7	34.8	0.90%
3	25	M	NO	YES	YES	YES	YES	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	9.2	29	1700	P71L20M9	28000	87.4	26.5	28.7	2.30%
4	40	F	YES	YES	YES	NO	NO	YES	NO	YES	NO	YES	NO	MIXED DIET	NO	5	15	400	P60L20	19000	88.2	27.1	28.6	0.70%
5	14	M	YES	YES	NO	NO	NO	YES	YES	NO	YES	YES	NO	MIXED DIET	NO	5.1	16	4000	P47L57E2	98000	91.1	28.9	31.5	1.50%
6	45	F	YES	YES	NO	YES	NO	NO	NO	NO	NO	YES	NO	MIXED DIET	NO	3.8	12	2500	P23L71M6	10000	92.1	29.9	32.5	0.40%
7	23	F	YES	YES	YES	NO	NO	NO	NO	YES	NO	NO	NO	MIXED DIET	NO	5.1	19	2600	P64l21e5	86000	74.2	20.2	27.3	2.80%
8	18	M	YES	YES	NO	NO	YES	YES	YES	YES	YES	YES	NO	MIXED DIET	NO	7.4	23	500	TOO LOW	18000	88.4	27.3	29.7	1.40%
9	14	M	YES	YES	NO	YES	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	3.9	12	1900	P14L82M4	2000	91.7	28.9	31.6	0.60%
10	27	M	NO	YES	YES	NO	NO	YES	YES	NO	NO	NO	YES	MIXED DIET	NO	6.7	20	3100	P50L32E12M6	86000	104.7	35.3	33.7	0.70%
11	40	F	YES	YES	NO	YES	NO	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	2.1	6	2700	P54L45	4000	88.9	29.2	32.8	1.50%
12	21	M	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	6.3	27	1700	P77L23	51000	77.5	23.4	26.5	1.90%
13	54	M	YES	YES	NO	NO	YES	YES	NO	NO	NO	YES	YES	MIXED DIET	NO	2.7	9	3400	P48L42M3	120000	81.1	25.2	29.7	1.40%
14	23	M	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	YES	MIXED DIET	NO	8	27	3400	P34L62	83000	93.2	27.4	29.4	1.00%
15	21	F	YES	YES	NO	YES	YES	YES	NO	NO	NO	YES	NO	VEGETERIAN	NO	3.4	11	3400	P26L74	5000	97.3	30.1	30.9	0.50%
16	39	M	NO	YES	YES	NO	YES	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	3.6	14	8000	P65L30E05	8000	81.5	27.5	29.2	2.50%
17	60	F	NO	YES	NO	NO	YES	YES	NO	YES	NO	NO	NO	MIXED DIET	NO	6.7	24	2300	P24L66M6E2	31000	97.7	20.1	25.9	0.90%
18	25	F	YES	YES	NO	YES	YES	YES	NO	NO	NO	NO	NO	MIXED DIET	NO	10.3	30	2800	P76L23	5000	88.4	28.4	30.4	1.10%
19	60	M	NO	YES	NO	NO	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	6.2	19	2400	P29L63	40000	91	28.3	30.3	0.70%
20	25	M	YES	YES	NO	NO	NO	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	2.9	9	1500	p51l33e16	10000	122.2	40.3	33	0.30%
21	29	M	YES	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	MIXED DIET	NO	11.4	34	3200	P62L36E2	48000	89.2	26.4	28.9	2.10%
22	60	F	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	6.9	21	3400	P70L22M8	86000	101	34	33.7	1.40%
23	38	M	YES	YES	NO	YES	YES	YES	NO	NO	NO	YES	YES	MIXED DIET	NO	3.2	10	1700	P33L67	2000	100	32.7	32.5	0.20%
24	50	F	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	7.2	21	3000	P45L47E8	94000	109.9	37.7	34.3	0.90%
25	33	M	YES	YES	NO	NO	NO	NO	YES	NO	NO	NO	YES	MIXED DIET	NO	4.3	17	3400	P67L33	118000	108.3	29.5	31.1	0.70%
26	25	M	NO	YES	NO	YES	YES	YES	NO	YES	NO	NO	NO	MIXED DIET	NO	11.4	35	3400	P70L21 E9	90000	94.5	24.4	27.8	2.60%
27	35	M	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	YES	MIXED DIET	NO	5.7	18	2700	P23L77	39000	111.7	35.2	31.5	0.70%
28	40	F	NO	YES	NO	YES	YES	YES	YES	NO	NO	YES	NO	VEGETERIAN	NO	1.6	5	2200	P23L77	4000	82.8	27.6	33.3	0.20%
29	58	M	NO	YES	YES	YES	YES	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	5.4	23	2600	P45L54	111,000	73.3	17.4	23.7	1.10%
30	55	F	NO	YES	YES	YES	YES	NO	YES	YES	NO	YES	NO	MIXED DIET	NO	3.6	16	2800	P54L30E16	105000	86.3	27.9	29.1	0.60%
31	53	F	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	9.2	33	3200	P57L34E4M5	121000	91.5	26.9	29.6	0.80%
32	25	F	YES	YES	NO	YES	YES	YES	YES	YES	NO	YES	NO	MIXED DIET	NO	8.8	26	2600	P35L65	6000	92.4	27.1	29.7	1.40%
33	17	M	YES	YES	YES	NO	NO	YES	NO	YES	NO	NO	NO	VEGETERIAN	NO	7.3	25	3100	P53L33M4	119000	105.8	31.1	33.2	1.10%

S.NO	AGE	SEX	FEVER	PALLOR	ICTERUS	BLEED	WT LOSS	ANOREXIA	LIVER	SPLEEN	LYMPHNODES	DYSPNEA	ALCOHOL	FOOD HABITS	SURGERY	HB	PCV	TC	DC	PLATELET	MCV	MCH	MCHC	RPI
34	15	M	YES	YES	NO	YES	YES	NO	NO	NO	NO	YES	NO	MIXED DIET	NO	5.1	16	2500	P25L75	12000	88.6	29	32.7	0.10%
35	50	F	YES	YES	NO	NO	YES	YES	YES	YES	NO	NO	NO	MIXED DIET	NO	6.7	21	2900	P52L40M8	81000	104.8	31.5	33.4	1.00%
36	36	F	NO	YES	NO	NO	YES	YES	YES	YES	NO	YES	NO	MIXED DIET	NO	5	17	3200	P69L22E4	96000	109.6	32.1	29.2	1.30%
37	28	F	YES	YES	NO	NO	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	10.2	30	2500	P67L27M4	90000	88.2	28.3	31.7	1.20%
38	45	F	YES	YES	YES	NO	YES	YES	YES	YES	NO	NO	NO	MIXED DIET	NO	5.4	21	2300	P58L28M4	78000	101.5	28.1	29.9	1.80%
39	42	M	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	5.5	18	1100	P30L56M14	18000	97.7	31.1	31.8	0.10%
40	42	F	NOYES	YES	NO	NO	NO	YES	NO	YES	NO	NO	NO	MIXED DIET	NO	10.4	33	3400	P55L28M17	25000	110.4	35	31.7	0.20%
41	35	M	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	YES	MIXED DIET	NO	9.7	32	3100	P71L18E01	50000	103.9	29.7	31.9	1.20%
42	18	F	YES	YES	NO	NO	NO	YES	YES	YES	NO	NO	NO	MIXED DIET	NO	2.2	10	2000	P43L53M4	47000	106.8	36.6	33.9	0.70%
43	26	M	YES	YES	YES	YES	NO	NO	NO	NO	NO	YES	NO	VEGETERIAN	NO	3.6	10	2000	P24L76	10000	79.2	27.5	34.7	0.40%
44	45	F	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	VEGETERIAN	NO	5	21	2900	P61L28M4	111000	114.2	36.8	34.9	0.90%
45	52	F	NO	YES	NO	NO	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	3.3	11	2300	P78L32	4000	111.5	34.4	30.8	0.60%
46	35	M	YES	YES	NO	YES	NO	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	5	16	2900	P47L49E4	6000	97.6	30.5	31.3	0.10%
47	39	F	YES	YES	NO	NO	YES	YES	NO	NO	NO	NO	NO	MIXED DIET	NO	7.4	29	3400	P57L25E10	75000	119.4	33.9	28.4	0.90%
48	55	F	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	6.9	22	3100	P50L28E22	71000	103.5	32.7	33.8	0.80%
49	31	M	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED DIET	NO	3.9	13	3300	P44L50ATY4	38000	127.3	39.4	31	1.00%
50	34	M	NO	YES	NO	NO	YES	YES	NO	YES	NO	NO	NO	MIXED DIET	NO	8.9	28	3900	P56L35E3	80000	87.9	27.1	30.5	2.20%
51	50	M	YES	YES	NO	YES	NO	YES	NO	NO	NO	YES	YES	MIXED DIET	NO	6.1	19	3600	P45L49E6	40000	83.2	26.3	31.6	0.30%
52	50	F	NO	YES	NO	NO	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	4.5	19	2600	P48L38M10	128000	67.7	16	23.6	0.90%
53	43	M	NO	YES	YES	YES	YES	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	6	22	2100	P41L30M34	85000	75.5	21.4	24.7	1.90%
54	26	M	YES	YES	NO	YES	NO	NO	NO	NO	NO	YES	NO	MIXED DIET	NO	2.7	8	1400	P24L76	8000	81.6	27.6	33.8	0.30%
55	36	F	NO	YES	NO	NO	YES	YES	YES	YES	NO	YES	NO	VEGETERIAN	NO	6.6	21	2900	P70L13E4	69000	113.5	32.7	34.2	0.80%
56	53	M	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	YES	MIXED DIET	NO	3.5	12	3100	P51L35E10	79000	108.3	31.1	32.2	1.20%
57	40	F	YES	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	MIXED DIET	NO	9.7	31	3200	P29L68M3	20000	107.4	34	31.7	0.50%
58	27	M	NO	YES	NO	NO	YES	YES	NO	NO	NO	NO	NO	MIXED DIET	YES	6.8	25	3100	P59L39E2	65000	111.3	32.3	34.1	0.90%
59	38	M	YES	YES	NO	NO	YES	YES	YES	YES	NO	YES	YES	MIXED DIET	NO	4.1	13	2000	P60L33E7	95000	112.7	34.7	30.8	1.20%
60	60	F	YES	YES	NO	YES	YES	YES	NO	NO	NO	YES	NO	MIXED DIET	NO	7.4	23	2000	P12L78	15000	93	30.2	32.5	0.20%
61	57	M	YES	YES	YES	NO	NO	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	8.8	25	3500	P62L30M6E2	44000	95.5	29.6	30.7	1.00%
62	45	F	YES	YES	NO	YES	YES	YES	YES	YES	YES	NO	NO	MIXED DIET	NO	3.4	11	700	TOO LOW	1000	91.1	28.4	29.5	1.50%
63	16	M	YES	YES	NO	YES	NO	YES	NO	NO	NO	NO	NO	MIXED DIET	NO	2.6	9	3500	P50L50	16000	114	33.3	29.2	0.20%
64	42	M	NO	YES	YES	YES	YES	YES	NO	YES	NO	YES	YES	MIXED DIET	NO	3	9	1800	P35L49	50000	93.7	29.1	31.1	1.40%
65	45	F	F	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	VEGETERIAN	NO	7.1	21	3500	P56L39E5	85000	112.2	32.4	28.9	0.60%

S.No	LDH	TB	OT	PT	ALP	TP	STOOL OCCULT BLOOD	HIV	VIRAL MARKERS	USG ABDOMEN	UPPER GI ENDOSCOPY	SE. IRON	SE FERRITIN	B12	FOL
1	1720	3.9	88	84	84	6	NO	NEG	NEG	NORMAL	NORMAL STUDY	234	170	140	6.5
2	556	0.8	32	44	51	6.2	NO	NEG	NEG	NORMAL	GASTRIC EROSIONS	345	256	185	7.2
3	230	5.5	260	185	275	4.6	POSITIVE	NEG	NEG	SPLENOMEGALY,CIRRHOSIS	ESOPHAGEAL VARICES+	65	90		
4	354	2.4	124	135	155	5.1	NO	NEG	NEG	SPLENOMEGALY	NORMAL STUDY				
5	145	1	35	45	51	4.9	NO	NEG	NEG	HEPATOMEGALY					
6	97	0.6	45	25	35	5.5	POSITIVE	NEG	NEG	NORMAL					
7	209	2	160	186	155	6.9	POSITIVE	NEG	NEG	CLD,SPLENOMEGALY	ESOPHAGEAL VARICES+	120	95		
8	178	0.7	77	65	45	4.9	NO	NEG	NEG	HSM+,LYMPHADENOPATHY					
9	78	0.9	33	35	54	5.2	NO	NEG	NEG	NORMAL					
10	453	1.8	66	76	102	5.8	NO	NEG	NEG	MILD HEPATOMEGALY	PANGASTRITIS,DUODENITIS	170	290	196	6.9
11	156	1.4	99	103	123	5.1	NO	NEG	NEG	NORMAL					
12	122	0.6	22	38	45	5.2	NO	NEG	NEG	NORMAL					
13	256	1.2	55	65	76	5.3	NO	POS	NEG	NORMAL	NORMAL STUDY	78	56		
14	765	0.7	45	41	32	5.9	NO	NEG	NEG	NORMAL	PANGASTRITIS,DUODENITIS	235	305	290	4.1
15	125	0.7	22	32	45	6.1	POSITIVE	NEG	NEG	NORMAL					
16	176	6.5	235	350	285	4.8	POSITIVE	NEG	HBsAg+	SPLENOMEGALY,CIRRHOSIS	ESOPHAGEAL AND GASTRIC VARICES	75	105		
17	890	0.8	67	76	83	5.8	NO	NEG	NEG	MILD SPLENOMEGALY	NORMAL STUDY	245	185	213	7.1
18	345	1.1	53	45	60	6.1	NO	NEG	NEG	NORMAL					
19	567	1.8	45	45	54	5.6	NO	NEG	NEG	NORMAL		170	250	330	11.3
20	90	1.1	34	23	45	5.9	POSITIVE	NEG	NEG	NORMAL					
21	231	0.5	10	24	35	6.1	NO	NEG	NEG	MILD HEPATOMEGALY					
22	550	1	35	35	75	5.6	NO	NEG	NEG	NORMAL	NORMAL STUDY	165	176	189	9.2
23	120	0.8	19	22	35	6.2	NO	NEG	NEG	NORMAL					
24	678	0.6	31	26	43	5.1	NO	NEG	NEG	NORMAL	NORMAL STUDY	250	185	232	9.7
25	345	0.9	83	92	45	5.3	POSITIVE	NEG	NEG	MILD HEPATOMEGALY	EROSIVE GASTRITIS	185	297	187	10.4
26	136	1.1	120	145	134	5.3	NO	NEG	NEG	SPLENOMEGALY	ESOPHAGEAL VARICES+	87	98		
27	478	0.5	42	55	45	5.7	NO	NEG	NEG	NORMAL	EROSIVE GASTRITIS	176	355	231	9.4
28	134	0.7	33	22	40	6.1	NO	NEG	NEG	MILD HEPATOMEGALY					
29	378	0.9	45	34	56	5.5	NO	NEG	NEG	SPLENOMEGALY		125	220	420	9.9
30	104	1.1	40	35	40	5.7	NO	NEG	NEG	SPLENOMEGALY		134	156		
31	778	0.9	44	34	35	5.2	NO	NEG	NEG	NORMAL	NORMAL STUDY	199	175	245	9.9
32	173	0.8	70	65	64	5.1	NO	NEG	NEG	HEPATOSPLENOMEGALY					
33	687	2.1	99	101	123	6.1	NO	NEG	NEG	MILD SPLENOMEGALY	NORMAL STUDY	194	290	199	10.2

S.No	LDH	TB	OT	PT	ALP	TP	STOOL OCCULT BLOOD	HIV	VIRAL MARKERS	USG ABDOMEN	UPPER GI ENDOSCOPY	SE. IRON	SE FERRITIN	B12	FOL
34	117	0.6	22	25	35	6.1	POSITIVE	NEG	NEG	NORMAL					
35	279	0.8	24	32	45	5.7	NO	NEG	NEG	NORMAL	NORMAL STUDY	150	185	201	6.2
36	525	1.1	45	54	65	5.9	NO	NEG	NEG	MILD HEPATOSPLENOMEGALY	NORMAL STUDY	165	156	340	4.2
37	245	0.7	35	25	45	4.9	NO	NEG	NEG	NORMAL	NORMAL STUDY	87	189		
38	184	4.5	255	215	325	5.1	NO	NEG	ANTI HCV +	HEPATOSPLENOMEGALY,PHT	ESOPHAGEAL VARICES,GASTRITIS	96	123		
39	112	1.2	43	40	53	5	POSITIVE	NEG	NEG	NORMAL					
40	95	0.9	22	33	54	6.1	NO	NEG	NEG	MILD SPLENOMEGALY					
41	420	1.1	85	75	92	5.9	POSITIVE	NEG	NEG	NORMAL	PANGASTRITIS,DUODENITIS	201	355	179	7.4
42	643	0.7	35	45	52	5.5	NO	NEG	NEG	HEPATOSPLENOMEGALY	ATROPHIC GASTRITIS.	168	176	142	5.6
43	118	2.5	88	94	105	5.2	NO	NEG	NEG	NORMAL					
44	665	0.6	44	53	34	5.4	NO	NEG	NEG	NORMAL	NORMAL STUDY	211	197	156	6.1
45	394	0.8	25	25	35	5.1	NO	NEG	NEG	NORMAL	NORMAL STUDY	176	188	440	3.4
46	101	0.4	17	24	35	5.7	POSITIVE	NEG	NEG	NORMAL					
47	756	0.8	34	45	52	5.4	NO	NEG	NEG	NORMAL	ATROPHIC GASTRITIS.	134	120	162	6.4
48	661	0.9	54	45	67	5	NO	NEG	NEG	NORMAL	NORMAL STUDY	183	211	220	9.2
49	290	0.6	25	35	42	5.1	POSITIVE	NEG	EG	NORMAL	GASTRITIS	175	299	165	11.1
50	220	0.8	157	187	206	5.6	POSITIVE	NEG	NEG	SPLENOMEGALY	ESOPHAGEAL AND FUNDAL VARICES	55	101		
51	135	0.8	40	43	35	5.2	POSITIVE	NEG	NEG	NORMAL					
52	890	0.7	22	30	28	5.4	NO	NEG	NEG	NORMAL		165	121	345	8.2
53	320	5.2	167	289	356	4.5	NO	NEG	NEG	SPLENOMEGALY,CIRRHOSIS	ESOPHAGEAL VARICES+,PANGASTRITIS	145	99		
54	145	1.2	33	44	40	5.3	NO	NEG	NEG	NORMAL					
55	990	1.1	45	55	52	6.2	NO	NEG	NEG	HEPATOSPLENOMEGALY	NORMAL STUDY	201	190	155	9.2
56	1034	0.8	105	163	171	5.6	NO	NEG	NEG	NORMAL	PANGASTRITIS,DUODENITIS	177	234	391	3.9
57	125	3.2	134	156	106	5.2	POSITIVE	NEG	NEG	NORMAL					
58	967	0.7	25	35	45	5.4	NO	NEG	NEG	NORMAL	GASTIC EROSIONS	164	246	211	7.9
59	927	0.9	94	83	122	5.2	NO	NEG	NEG	MILD HEPATOSPLENOMEGALY	PANGASTRITIS,DUODENITIS	171	288	181	12.2
60	118	0.5	16	19	25	6.1	NO	NEG	NEG	NORMAL					
61	885	1.2	44	45	67	4.9	NO	NEG	NEG	NORMAL		189	250	356	10.2
62	201	0.8	35	40	45	4.9	NO	NEG	NEG	HEPATOSPLENOMEGALY					
63	101	0.7	25	25	40	5.2	POSITIVE	NEG	NEG	NORMAL					
64	196	3.8	256	345	325	4.6	NO	NEG	NEG	SPLENOMEGALY,CIRRHOSIS	ESOPHAGEAL VARICES+,GASTRITIS	144	55		
65	765	0.5	15	35	45	5.5	NO	NEG	NEG	NORMAL	NORMAL STUDY	256	195	241	10.2

S.NO.	T4	TSH	PERIPHERAL SMEAR
1	1.2	2.35	ANISOPOIKILOCYTOSIS+,MACROCYTIC RBC S,HYPERSEGMENTED NEUTROPHILS+,RETICS INCREASED
2	1.4	1.34	MACROCYTIC/NORMOCYTIC RBC S,ANISOPOIKILOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+
3			MICROCYTIC HYPOCHROMIC RBCS.
4			MICROCYTIC/HYPOCHROMIC
5			MYELOID BLASTS 85% PRESENT
6			PANCYTOPENIA
7			MICROCYTIC/HYPOCHROMIC
8			MICROCYTIC HYPOCHROMIC RBCS,PLATELETS DECREASED,WBCS DECREASED,BLASTS+
9			SEVERE PANCYTOPENIA
10	0.75	0.91	MACROCYTIC RBC S,ANISOPOIKILOCYTOSIS,PLATELETS DECREASED,HYPERSEGMENTED NEUTROPHIL+,TEAR DROP CELLS,
11			MYELOID BLASTS+
12			MICRO HYPO RBCS,TARGET CELLS
13			MICRO,HYPO rbcs NORMO RBCS
14	0.56	1.21	ANISOPOIKILOCYTOSIS,PLATELETS DECRESED,LYMPHOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+
15			MICROCYTIC/HYPOCHROMIC RBCs PRESENT
16			micro,hypo rbcs target cells,reticulocytosis.
17	0.09	6.25	MACROCYTIC RBCS,ANISOPOIKILOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+
18			BLASTS 10%,TLC DECREASED.PLT DECREASED
19			PANCYTOPENIA,OCC ATYPICAL CELLS,ANISOPOIKILOCYTOSIS,GIANT PLATELETS.
20			MACROCYTIC RBCS,DECREASED WBCS,
21			NORMO,NORMO RBCS
22	0.41	3.23	MACROCYTIC RBC S,ANISOPOIKILOCYTOSIS,PLATELETS DECREASED,ERYTHROBLAST+,ROULEAUX FORMATION+,HYPERSEGMENTED POLYMORHS+
23			MICROCYTIC/HYPOCHROMIC
24	0.06	7.23	MACROCYTIC/NORMOCYTIC RBC S,ANISOPOIKILOCYTOSIS,FEW ELLIPTOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+,INCREASED RETIC
25	1.23	3.45	MILD ANISOPOIKILOCYTOSIS,SMALL PLATELET CLUMPS+,HYPERSEGMENTED NEUTROPHILS+
26			MICRO HYPO/NORMO RBCS,RETICULOCYTOSIS+
27	1.56	4.35	MACROCYTIC RBCS, FEW TARGET CELLS,ANISOPOIKILOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+,PLATELETS DECREASED,WBC MOD RED.
28			rbcs sparsely distributed,severe mchc with anisopoikilocytosis,wbcs dec,platelets dec.
29			MICRO HYPO/NORMO RBCS
30			MICRO HYPO/NORMO RBCS,ANISOPOIKILOCYTOSIS,TEAR DROP SHAPED CELLS.
31	0.05	8.34	NORMO/MACROCYTIC RBCS,ANISOPOIKILOCYTOSIS,ERYTHROBLASTS,HYPERSEGMENTED NEUTROPHILS+,PLT LOW,HSPS+
32			MYELOID BLASTS+,TLC DECREASED,PLT DECREASED
33	1.25	3.14	NORMO/MACROCYTIC RBCS,ANISOPOIKILOCYTOSIS,ERYTHROBLASTS+,PLT LOW,HYPERSEGMENTED POLYMORPHS+

S.NO.	T4	TSH	PERIPHERAL SMEAR
34			NORMO/HYPO RBCS
35	1.13	2.91	POIKILOCYTOSIS+,MILD ROULEAUX FORMATION,HYPERSEGMENTED NEUTROPHILS,PLATELETS DECREASED.
36	1.34	3.96	MACROCYTIC RBCS,HYPERSEGMENTED NEUTROPHILS+,ERYTHROBLASTS,INCREASED RETIC COUNT,PLT DECREASED
37			MICRO HYPO/NORMO RBCS
38			MICRO HYPO/NORMO RBCS
39			severe microcytic hypochromic rbcs,anisopoikilocytosis,wbc decreased,platelets decreased
40			NCNC rbcs,mild anisopoikilocytosis,tear drop cells seen.wbc dec,plt dec.
41	0.81	3.19	NORMOCYTIC/NORMOCHROMIC,MACROCYTIC RBCS,ANISIPOIKILOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+,PLT DECREASED
42	1.52	2.76	ANISOPOILKILOCYTOSIS,RETICULOCYTOSIS,HYPERSEGMENTED NEUTROPHILS+,PLT DECREASED,WBC DECREASED
43			MICRO,HYPO RBCS
44	1.45	3.56	MACROCYTES+,ERYTHROBLASTS+,HYPERSEGMENTED POLYMORPHS,ANISOPOIKILOCYTOSIS+.PLATELETS DECREASED,CLUMPS+
45	1.23	2.91	ANISOPOIKILOCYTOSIS,MACROCYTES
46			MICRO,HYPO RBCS
47	0.91	4.1	ANISOPOIKILOCYTOSIS,PLATELETS DECRESED,HYPERSEGMENTED NEUTROPHILS+
48	0.12	10.5	ANISOPOIKILOCYTOSIS,PLATELETS DECRESED,HYPERSEGMENTED NEUTROPHILS+
49	1.67	2.96	MACROCYTES+,ERYTHROBLASTS+,HYPERSEGMENTED POLYMORPHS,ANISOPOIKILOCYTOSIS+.PLATELETS DECREASED,CLUMPS+
50			MICRO HYPO RBCS TARGET CELLS,RETICULOCYTOSIS+
51			microcytic hypochromic rbcs,platelets decreased,wbc s decreased.
52			gross microcytic hypochromic rbcs,platelets mildly dec,tlc mod dec,atypical cells.
53			MICROCYTIC HYPOCHROMIC RBCS,RETICULOCYTOSIS+.
54			microcytic hypochromic rbcs,platelets decreased,wbc s decreased.
55	1.58	4.1	ANISOPOIKILOCYTOSIS,PLATELETS DECRESED,HYPERSEGMENTED NEUTROPHILS+
56	1.61	2.17	HYPERSEGMENTED POLYMORPHS,MACROCYTES+
57			MICRO,HYPO RBCS
58	1.09	1.91	MACROCYTES+,ANISOPOIKILOCYTOSIS
59	0.98	2.56	ANISOPOIKILOCYTOSIS,PLATELETS DECRESED,HYPERSEGMENTED NEUTROPHILS+
60			microcytic hypochromic rbcs,platelets decreased,wbc s decreased.
61			MICRO HYPO RBCS TARGET CELLS
62			BLASTS+,TLC DECREASED.PLT DECREASED
63			ANISOPOILILOCYTOSIS
64			MICRO HYPO RBCS,ELLIPTOCYTOSIS.
65	1.59	3.23	MACROCYTES+,ERYTHROBLASTS+,HYPERSEGMENTED POLYMORPHS,ANISOPOIKILOCYTOSIS+.PLATELETS DECREASED,CLUMPS+

S.NO	BONE MARROW STUDY	DIAGNOSIS
1	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA+	MEGALOBLASTIC ANEMIA
2	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
3	HYPERCELLULAR,NORMAL PRECURSORS	HYPERSPLENISM/CLD
4	hypocellular,fibrosis present,decreased myeloid precursors	SLE/CTD
5	MYELOID leukemic blasts present	ACUTE MYELOID LEUKEMIA
6	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
7	NORMOCEL,MEGAKAR ADEQ	HYPERSPLENISM/CLD
8	LYMPHOID leukemic blasts present	ACUTE LYMPHOID LEUKEMIA
9	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
10	HYPERCELLULAR,MEGALOBLASTIC,LARGE MEGAKARYOCYTES+	MEGALOBLASTIC ANEMIA
11	leukemic blasts present	ACUTE MYELOID LEUKEMIA
12	normocellular,precursors normal	VIRAL INFECTION INDUCED
13	hypocellular,occ megakaryocyte with bare nuclei,dyserythropoiesis,mod decrease in erythroid and myeloid progenito	HIV INDUCED PANCYTOPENIA
14	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA+	MEGALOBLASTIC ANEMIA
15	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
16	HYPERCELLULAR,NORMAL PRECURSORS	HYPERSPLENISM/CLD
17	HYPERCELLULAR,LARGE MEGAKARYOCYTES PRESENT HYPERLOBULATED	MEGALOBLASTIC ANEMIA
18	immature myeloid blasts present	ACUTE MYELOID LEUKEMIA
19	hypercellular marrow,fragmented erythroblasts+	MYELODYSPLASTIC SYNDROME
20	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
21	normocellular,precursors normal	VIRAL INFECTION INDUCED
22	HYPERCELLULAR,MEGALOBLASTIC,FEW GIANT METAMYELOCYTE SEEN	MEGALOBLASTIC ANEMIA
23	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
24	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
25	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
26	hypercellular marrow, normal precursors	HYPERSPLENISM/EHPO
27	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
28	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
29	hypercellular marrow,ringed sideroblasts+,DYSPLASTIC	MYELODYSPLASTIC SYNDROME
30	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA+	MEGALOBLASTIC ANEMIA
31	immature myeloid blasts present	ACUTE MYELOID LEUKEMIA
32	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
33	hypocellular marrow,replaced by fat	APLASTIC ANEMIA

S.NO.	BONE MARROW STUDY	DIAGNOSIS
34	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA+,LARGE MEGAKARYOCYTES PRESENT	MEGALOBLASTIC ANEMIA
35	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
36	BONE MARROW STUDY	DIAGNOSIS
37	hypocellular marrow.	SLE/CTD
38	ADEQUATE CELLULARITY WITH MILD TO MODERATE MEGALOBLASTIC CHANGES.	HYPERSPLENISM/CLD
39	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
40	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
41	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
42	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
43	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
44	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA	MEGALOBLASTIC ANEMIA
45	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
46	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
47	HYPERCELLULAR,MEGALOBLASTIC CHANGES PRESENT	MEGALOBLASTIC ANEMIA
48	HYPERCELLULAR,MEGALOBLASTIC,LARGE MEGAKARYOCYTES+	MEGALOBLASTIC ANEMIA
49	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
50	hypercellular marrow normal precursors.	HYPERSPLENISM/EHPO
51	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
52	hypercellular,dyserythropoietic,abnormal megakaryocytes,BINUCLEATED ERYTHROID PRECURSORS	MYELODYSPLASTIC SYNDROME
53	hypercellular marrow normal precursors.	HYPERSPLENISM/CLD
54	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
55	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
56	HYPERCELLULAR,MEGALOBLASTIC,LARGE MEGAKARYOCYTES+	MEGALOBLASTIC ANEMIA
57	HYPERCELLULAR,MEGALOBLASTIC,ERYTHROID HYPERPLASIA	APLASTIC ANEMIA
58	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
59	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA
60	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
61	hypercellular,dyserythropoietic,abnormal megakaryocytes,RINGED SIDEROBLASTS PRESENT	MYELODYSPLASTIC SYNDROME
62	lymphoid blasts present.	ACUTE LYMPHOID LEUKEMIA
63	hypocellular marrow,replaced by fat	APLASTIC ANEMIA
64	hypercellular marrow normal precursors.	HYPERSPLENISM/CLD
65	HYPERCELLULAR,MEGALOBLASTIC	MEGALOBLASTIC ANEMIA

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INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-600 003

Telephone 25363970
Fax 044 2535115
Dated : 12.05.2010

L.Dis.No.14597/ME5/Ethics Dean/MMC/2010

Title of the work : "A study on the clinical and Etiological profile of patients with pancytopenia."

Principal Investigator : Dr. Myvizhiselvi. M
Designation : PG in MD General Medicine
Department : Madras Medical College & GGH, Ch-3.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
4. You should not deviate form the area of the work for which you applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulation of the institution(s).
7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC,CHENNAI

CHAIRMAN
IEC,MMC, CHENNAI

DEAN
MADRAS MEDICAL COLLEGE,
CHENNAI -3